

The National Nanotechnology Initiative

STRATEGY FOR NANOTECHNOLOGY-RELATED ENVIRONMENTAL, HEALTH, AND SAFETY RESEARCH



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About this document

This document outlines the NNI strategy for nanotechnology-related environmental, health, and safety (EHS) research. It includes an analysis of the EHS research needs outlined in the previously published NNI document, *Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials* (September 2006) and a summary of the current NNI EHS research portfolio, divided into five primary research categories: (1) Instrumentation, Metrology, and Analytical Methods; (2) Nanomaterials and Human Health; (3) Nanomaterials and the Environment; (4) Human and Environmental Exposure Assessment; and (5) Risk Management Methods. The document also includes an analysis of the strengths, weaknesses, and gaps in the current NNI research portfolio, a recommended framework for addressing the identified research needs, as well as a recommended implementation and adaptive management process. Tables showing research projects funded in 2006 by the NNI agencies in each of the five EHS research categories are included as an appendix.

About the cover

Idealized representation of a scanning tunneling microscope image showing closed chains of C60 molecules, represented by the light-colored lines, around islands of silver on a flat, clean surface of silver. Cover design by Nicolle Rager Fuller, Sayo Arts, Washington, DC.

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National Nanotechnology Initiative
**Strategy for Nanotechnology-Related
Environmental, Health, and Safety Research**



February 2008

Subcommittee on Nanoscale Science, Engineering, and Technology
Committee on Technology
National Science and Technology Council

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February 13, 2008

Dear Colleague:

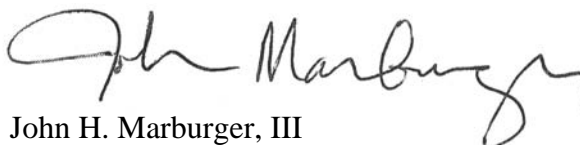
Nanotechnology is revolutionizing the creation and production of new materials with unprecedented functional properties. Since its inception, the National Nanotechnology Initiative (NNI) has supported research on the potential environmental and health effects of these new materials as an essential part of its broad base of fundamental nanotechnology research and development.

Following on previous work to identify and prioritize the research needs for nanotechnology-related environmental, health, and safety (EHS) issues, this *Strategy for Nanotechnology-Related Environmental, Health, and Safety Research* is the culmination of a comprehensive effort led by the Nanotechnology Environmental and Health Implications (NEHI) Working Group under the National Science and Technology Council's Nanoscale Science, Engineering, and Technology (NSET) Subcommittee. The report lays out a framework to guide and inform agency efforts to address prioritized research areas and to sustain a diverse program to advance knowledge and support risk decision making—both of which are essential for the responsible development of nanotechnology. The strategy reflects a strong consensus among the NNI agencies, defining clear roles consistent with their respective missions for implementing the strategy under the auspices of the strong interagency coordination that has been a hallmark of the NNI from the beginning.

NNI agency funding of research to enable sound risk assessment and risk management of nanoscale materials and products is increasing at a higher rate than any other component of NNI research. In FY 2009, the President's budget requests \$76 million in research primarily addressing potential risks to health and environment posed by nanotechnology—double the actual expenditures in 2006. This amount does not include substantial research on instrumentation and metrology and on fundamental biological interactions upon exposure to nanomaterials—all of which are also important to advancing understanding of nano-EHS issues.

The United States leads the world in coordination and investment for nanotechnology development and invests significantly more than any other country in research to understand the potential health and safety issues of engineered nanomaterials. Carrying out this research remains a core commitment of the NNI.

Sincerely,

A handwritten signature in dark ink, appearing to read "John Marburger, III". The signature is fluid and cursive, with the last name "Marburger" being more prominent.

John H. Marburger, III
Director

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Executive Summary

The ability to control matter at the nanometer scale is leading to technological advances in many areas, including energy, medicine, and the environment. These advances are based on the fact that at the nanoscale, materials have different properties than in macroscopic or bulk form. The novel behavior of nanomaterials may also pose risks to human health and the environment. To better understand these potential risks, the National Nanotechnology Initiative (NNI), which encompasses activities related to nanotechnology across the Federal Government, has included, as a critical, integrated component since its inception, research to understand potential risks associated with nanotechnology.

NNI research on environmental, health, and safety (EHS) aspects of nanomaterials has increased steadily. Between fiscal year (FY) 2005, the first year for which estimates are available, and the President's request for 2009, the NNI will invest an estimated \$254 million in research that is primarily aimed at understanding the risks posed by nanomaterials. This funding and corresponding effort to advance understanding of nanotechnology-related environmental, health, and safety issues is leveraged by a significant amount of additional investment in instrumentation, metrology, facilities, and fundamental materials research. This research and other NNI activities are coordinated by the Nanotechnology Environmental and Health Implications (NEHI) Working Group under the National Science and Technology Council's Nanoscale Science, Engineering, and Technology (NSET) Subcommittee.

This document describes the NNI strategy for addressing priority research on the environment, health, and safety (EHS) aspects of nanomaterials that have been identified in previous reports. Establishing this strategy is the next step in an interagency effort that has been underway for a number of years. This effort has entailed identifying and prioritizing EHS research for nanomaterials; analyzing the current research portfolio in detail; performing a gap analysis to determine areas requiring emphasis; and developing a strategy to address these areas and to sustain the diverse program aimed at advancing knowledge and supporting risk decision making.

Why Have an EHS Research Strategy?

Since its inception, the NNI member agencies have supported research to safely develop and apply nanotechnology for societal benefit and economic growth, as well as research to better protect public health and the environment. By integrating the results of such research, the NNI aims to maximize the benefits of this new technology at the same time as it is developing an understanding of any potential risks and means to manage such risks. The NEHI Working Group developed this nanotechnology-related EHS research strategy to accelerate progress in research to protect public health and the environment, and to fill gaps in, and—with the growing level of effort worldwide—to avoid unnecessary duplication of, such research. The approach is driven by the breadth of issues, from transport in the environment and effects on human health to managing risks and the overarching need to measure and characterize nanomaterials in various environments. Addressing such a range of issues requires participation by and coordination among the various NNI agencies with diverse competencies and expertise.

How Was the Strategy Developed?

In order to guide the Federal EHS research program, the NEHI Working Group performed a thorough analysis in each of five research categories of existing research. The existing portfolio of research is based in large part on detailed data collected for fiscal year 2006, which is included as Appendix A to this report. In FY 2006, the Federal Government invested \$68 million in 246 projects at seven agencies. Although the five research categories were not prioritized with respect to each other, there is consensus among members of the NEHI Working Group that research in the Instrumentation, Metrology, and Analytical Methods category is cross-cutting, supporting research in

every other category, and therefore is generally a high priority. Among the five research categories, the FY 2006 distribution of projects and spending was: 78 projects (\$26.6 million) in Instrumentation, Metrology, and Analytical Methods; 100 projects (\$24.1 million) in Nanomaterials and Human Health; 49 projects (\$12.7 million) in Nanomaterials and the Environment; five projects (\$1.1 million) in Human and Environmental Exposure Assessment; and 14 projects (\$3.3 million) in Risk Management Methods. In short, the analysis demonstrated that the Federal Government is supporting more EHS research than has been previously identified, and the research is well-distributed across key priority areas.

In addition to identifying areas of weakness and gaps, the working group developed timelines and sequencing for key research activities in order to gain the greatest and most immediate benefit for nanotechnology development broadly and risk management in particular. Recommended sequencing is based on immediacy of needs and whether additional research capacity or prerequisite research is required before research in a particular area can be initiated.

Who Will Implement the Research Strategy?

This strategy will be implemented through a coordinated interagency approach. In addition to the existing coordination of activities through the NEHI Working Group, the EHS research strategy specifies the roles of agencies as contributors to—through funding of EHS research, individually and jointly, that aligns with agency missions—or users of the results of EHS research and information. The strategy also identifies the agencies that will act as coordinators in the five EHS research categories:

- Instrumentation, Metrology, and Analytical Methods—National Institute for Standards and Technology (NIST)
- Nanomaterials and Human Health—National Institutes of Health (NIH)
- Nanomaterials and the Environment—Environmental Protection Agency (EPA)
- Human and Environmental Exposure Assessment—National Institute for Occupational Safety and Health (NIOSH)
- Risk Management Methods—Food and Drug Administration (FDA) and EPA

How Will the Strategy Be Implemented?

To implement the strategy, the NEHI Working Group and NNI agencies individually and jointly will, within the scope of their agency missions, priorities, and resources:

- Support a broad base of research that facilitates risk-based decision making and development of nanotechnology-based applications for improving the environment and health
- Coordinate agency efforts to address priority research needs, with a focus on weaknesses and gaps, identifying opportunities for collaboration and joint development and use of resources, where appropriate
- Hold workshops to assess progress and evolving needs in each of the five research categories
- Facilitate partnerships with industry
- Coordinate and support efforts internationally, particularly at the Organisation for Economic Cooperation and Development (OECD) and the International Organization for Standardization (ISO)
- Support development of consensus-based documentary standards
- Facilitate wide dissemination of research results and other non-proprietary EHS information

The strategy presented here is based on the state of science today; however, the field of nanotechnology is extremely dynamic. As nanotechnology EHS research and knowledge continue to grow, needs and priorities will evolve. Accordingly, this plan will be reviewed and updated as research progresses. Through continued coordination among the Federal agencies and with other governments, industry, and other stakeholders, the NNI will ensure that the United States remains a leader in the responsible development of nanotechnology.

I. Introduction and Background

Environmental, Health, and Safety Research and the National Nanotechnology Initiative

Nanotechnology encompasses an increasing number of activities based on the ability to measure, see, and control matter at the scale of nanometers. Nanoscale circuitry is already in cell phones and other electronic products on the market today. Many applications that are envisioned will take advantage of the fact that at the nanoscale materials have different chemical and physical properties than materials at larger scales. Also, there is potential for nanosized particles to be transported through cell walls and other biological barriers in ways that are different from their macroscale counterparts. These properties can be used to make better batteries, to deliver drugs where they are needed, and to clean contaminated soil and groundwater.

The National Nanotechnology Initiative (NNI) is the Federal Government's multiagency, multidisciplinary nanotechnology research and development (R&D) program. Established in fiscal year 2001, the NNI serves as a locus for communication, cooperation, and collaboration among the participating Federal agencies and provides a framework of shared goals, priorities, and strategies. The goals of the NNI are to advance a world-class R&D program; to foster the transfer of new technologies into products for commercial and public benefit; to develop and sustain educational resources, a skilled workforce, and the supporting infrastructure and tools to advance nanotechnology; and to support responsible development of nanotechnology.

Responsible development of nanotechnology includes supporting fundamental discovery-based research as well as targeted research and other activities to understand potential risks associated with the manufacture and use of engineered nanoscale materials. Since the inception of the NNI, the participating agencies have supported research to safely develop and apply nanotechnology for societal benefit and economic growth, as well as research to better protect public health and the environment. By integrating the results of such research, the NNI aims to ensure the benefits of this new technology are maximized within a coordinated research framework that emphasizes understanding and prioritizing potential risks as well as the means to manage such risks.

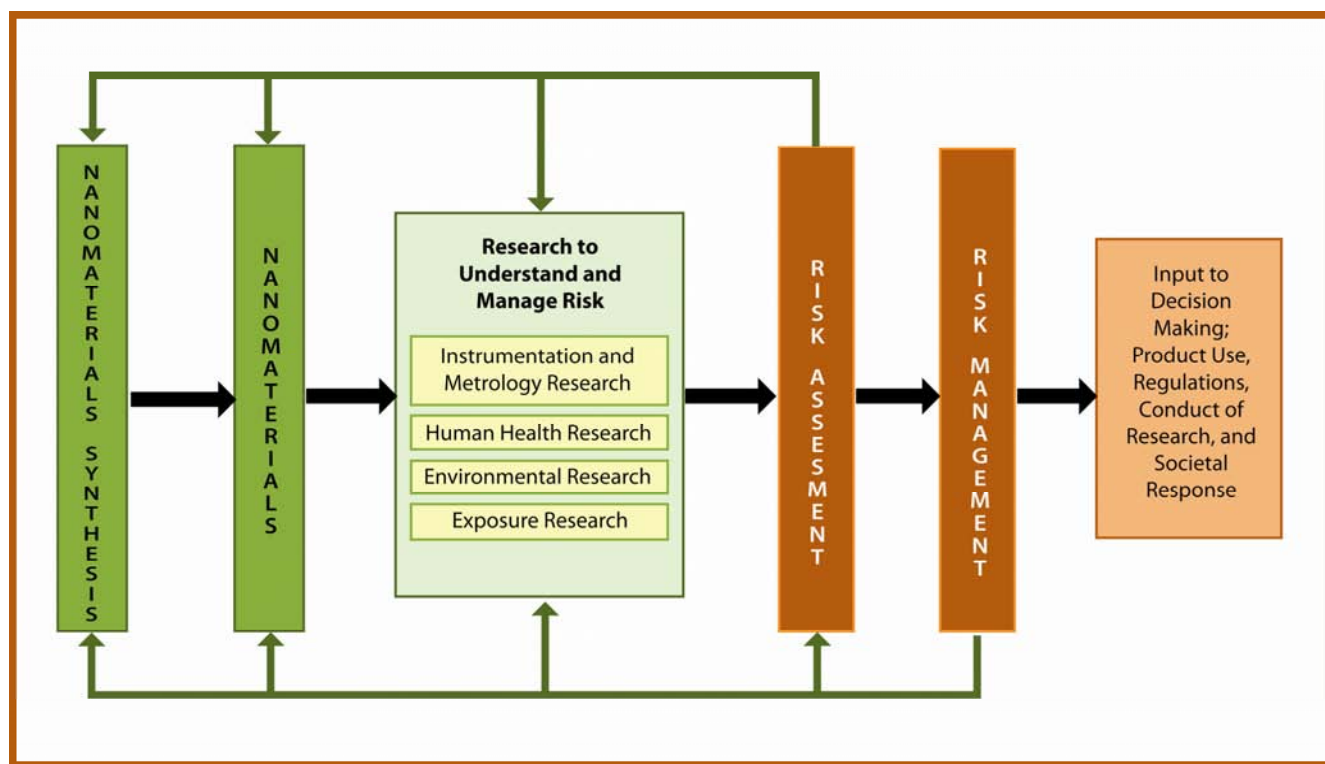
Nanotechnology-related environmental, health, and safety (EHS) research is an essential component of the NNI's coordinated research framework. EHS research is focused in particular on understanding general mechanisms of biological interaction with nanomaterials and on developing broadly useful tools and tests for characterizing and measuring nanomaterials in various environments, including in the body. The relevance of this research is in understanding the effects of and addressing the potential implications of engineered, incidental, and natural nanomaterials; supporting sustainable development; removing contaminants from soil and water; and preparing for the new generation of nanoproducts. Nanotechnology-related EHS research is also informed and influenced by all other components of the broader NNI research portfolio including research on fundamental nanoscale phenomena and processes; nanomaterials; nanoscale devices and systems; instrumentation, metrology, and standards; nanomanufacturing; and societal dimensions (ethical, legal, and other societal issues).

The discovery-based science agencies have been establishing a broad and strong foundation of basic research to expand current understanding of health and environmental implications. This report focuses on research that builds on this strong foundation to support risk assessment and risk management of nanoscale materials. Development of specific EHS research programs—by NNI agencies singly or jointly—is informed largely, but not exclusively, by the research and information needs of agencies with regulatory and oversight responsibilities. Input about the needs of regulatory decision makers expedites the development of information to support both risk assessment and risk management of nanomaterials; and basic research and discovery of new materials and new properties can lead to

significant changes in the context for risk assessment and management (Figure 1). Thus, a coordinated risk management approach is particularly important considering the multiagency nature of the NNI EHS research effort.

Understanding the potential risks of nanomaterials to human health and the environment involves research on a number of processes, which are shown schematically in Figure 2. Not every process will be equally important for every situation in which a nanomaterial enters the environment. For example, the processes that affect a nanomaterial that is used in a cosmetic will be different from those that affect a nanomaterial that is used in an industrial process such as polishing, or one that is incorporated into a bicycle frame. The framework shown in Figure 2 is not intended to reflect all the relationships and lines of feedback between the various components of EHS research but is helpful for organizing the variety of research activities needed to support risk assessment and risk management decisions.

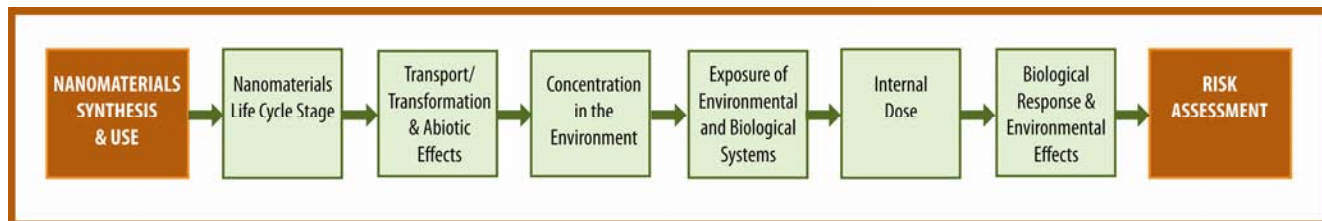
Figure 1. Role of nanotechnology-related EHS research in risk management of nanomaterials



As shown in Figure 2, EHS research must take into consideration the life cycle stage of the nanomaterial—e.g., manufacturing, incorporation into an integrated product, consumer use, and recycling or disposal. Nanomaterials released into the environment undergo various forms of transport and transformation and may cause abiotic effects, such as modification of atmospheric, soil, or water chemistry. The concentration of nanomaterial in the environment depends on factors such as the nature and amount of material released, physical and chemical conditions, and time. Once a nanomaterial is dispersed, biological or environmental systems may be exposed to the nanomaterial. Such contact may or may not lead to uptake by the system, resulting in an internal dose that may, in turn, cause a biological response and/or an ecological effect. Collective exposure of individuals leads to effects at the population, community, or ecosystem level. Biological and ecological effects may in turn lead to abiotic effects or may impact further transformation or transport of nanomaterials that are still in the environment or that are newly released.

Research on human health effects of nanomaterials follows a similar framework but has several additional considerations. Exposure to nanomaterials may occur unintentionally in the environment, as described above, or through intentional applications, such as cosmetics, therapeutics, or tissue implants, or potentially through ingestion of food. Once in the body, *in vivo* transport and transformation would need to be assessed, and biological response would need to be evaluated in terms of external dose, uptake by route of exposure, and internal dose.

Figure 2. Simplified framework for research related to EHS risk assessment of nanomaterials



Research programs that will help to understand many of the processes outlined above have been established at multiple agencies, based on expertise, information needs, respective missions and priorities, and merits of the proposed research. Where appropriate, joint programs among agencies with mutual interests have been put in place to leverage investments. In addition, activities other than research are ongoing that help to address issues related to potential EHS implications of nanomaterials. Examples include development of the cross-agency Food and Drug Administration (FDA) Nanotechnology Task Force report,¹ development of the Environmental Protection Agency (EPA) white paper² outlining agency-specific research needs and priorities, and organization of various public meetings, peer review panels, and workshops. Although not included in the research portfolio, these efforts are essential to furthering nanotechnology EHS research efforts and are key elements in the overall Federal NNI R&D program.

The Federal Government is not the only stakeholder with an interest and a role in research related to understanding potential EHS risks associated with nanomaterials. Businesses that manufacture or use nanomaterials have responsibilities for product and worker safety. Other economies, including Taiwan, Japan, China, and the European Union and its member states, are all beginning to invest in this area of research, although the United States appears to have a substantially larger investment in nanotechnology-related EHS research to date. NNI EHS research should be coordinated with these outside efforts so as to maximize its value to Federal agencies and to those other entities with needs for the information and knowledge.

Interagency coordination among the NNI agencies occurs within the Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the National Science and Technology Council's Committee on Technology. Under the NSET Subcommittee, the Nanotechnology Environmental and Health Implications (NEHI) Working Group provides a forum for agencies to coordinate their individual agency activities related to understanding potential risks of nanotechnology. The interagency activities are supported by the full-time staff of the National Nanotechnology Coordination Office.

The NEHI Working Group has developed this document to accelerate progress in nanotechnology-related EHS research, avoid gaps, and—considering the growing level of effort—avoid unnecessary duplication. Section II includes a summary of the NNI EHS research portfolio in FY 2006; including an analysis to determine strengths, weaknesses, and gaps of that portfolio. The analysis is conducted in terms of the five basic priority research categories

¹ <http://www.fda.gov/nanotechnology/taskforce/report2007.html>

² <http://www.epa.gov/OSA/pdfs/nanotech/epa-nanotechnology-whitepaper-0207.pdf>

spelled out in the September 2006 NNI document, *Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials*,³ hereafter referred to as the EHS Research Needs document. Section III provides a framework for addressing the research needed to support risk assessment and risk management of nanomaterials and a plan for implementing and managing the Federal EHS research program given the rapidly evolving state of knowledge. Agencies whose missions support nanomaterial research may use this document to better understand where their activities fit into the overall strategy. Moreover, agencies can use it to identify opportunities for collaboration and cooperation, and manage their relationships with other agencies and their research. Appendix A provides detailed information on the portfolio of Federally funded nanotechnology EHS research in FY 2006.

Process for Developing a Research Strategy

1. Identify priority needs

The research strategy described in this document builds upon two earlier NNI reports that identify and prioritize EHS research needs: first, the September 2006 EHS Research Needs document referred to above outlined the research and information needed to support scientifically sound risk assessment and risk management decision making. The needs were identified with input from the Federal agencies with responsibility for oversight of the research, development, manufacture, import, sale, or use of nanomaterials and the products and processes in which they are used. The needs were also informed by input from non-Federal experts on risk assessment issues and by relevant publications on the topic and are grouped in five categories. Second, in August 2007, an interim document,⁴ hereafter referred to as the Interim EHS Research Priorities document, which updated and prioritized the top five research needs in each category, was released for public comment. The prioritized research needs by category are shown in Table 1. *Prioritized research needs, as used in this document, refer to research that should be emphasized at specified time intervals over the course of implementing the NNI EHS research strategy.*

2. Assess existing research

In addition to developing a prioritized set of research needs, the NEHI Working Group worked with the Office of Management and Budget (OMB) to collect a “snapshot” of detailed information on nanotechnology-related EHS research already underway. These data were used to help identify gaps or weaknesses that a research strategy should address. The agencies reported information for research funded in fiscal year (FY) 2006 related to the needs listed in the 2006 EHS Research Needs document. The project level information is tabulated in Appendix A and is available online in a searchable format at <http://www.nano.gov/html/society/EHSprojects.html>. Summaries and analyses of the research funded in 2006 are in Section II of this report.

The reader should note the difference between the scopes of the research included in the data reported here for FY 2006 and that reported as “EHS research” in the annual NNI budget supplements to the President’s Budget since FY 2005. The annual NNI supplement to the President’s Budget reports funding for research that is “primarily aimed at understanding risks posed by nanomaterials.” Data presented in Appendix A and elsewhere in this report also include research that supports the five research categories but that may not be primarily aimed at understanding potential risks of engineered nanomaterials. The additional research captured by this approach is predominantly of two types: (1) instrumentation and metrology research that enables characterization and measurements vital to the development and risk assessment of nanomaterials, and (2) portions of medical application-oriented research that assesses possible toxicity of nanomaterials being considered for use in the human body.

³ http://www.nano.gov/NNI_EHS_research_needs.pdf

⁴ http://www.nano.gov/Prioritization_EHS_Research_Needs_Engineered_Nanoscale_Materials.pdf

The NEHI Working Group established five task force groups, one for each research category, comprising EHS experts from relevant agencies. The task forces reviewed the FY 2006 data carefully for quality and to ensure that projects were properly categorized.

3. Analyze strengths and weaknesses

Once the project categorization was final, the task forces analyzed the portfolio of projects in each category to determine the balance of effort among the priority research needs and to identify strengths, weaknesses—i.e., research need areas that should receive greater emphasis—and gaps for the research category as a whole. In addition to tabulating the number of projects and total funding in each category and estimating the 2006 funding and number of projects for the research needs of each respective category, the task forces considered the breadth of research, such as variety of nanomaterials or routes of exposure, being investigated. They also considered whether the materials being researched are those entering commerce or likely to be used in greatest volume, and whether the types of exposures being investigated are relevant to real-world situations. They also analyzed the timing for increased emphasis on particular needs. Finally, they considered agency-specific research and regulatory needs in this process. Delaying greater investment in certain areas is recommended where the research depends on results from, or progress in, other areas, or the need to develop capacity for a specific type of research.

The success of the strategy outlined in this EHS research strategy document depends on the collective efforts of the NNI agencies through their individual and joint activities coordinated by the NEHI Working Group and the NSET Subcommittee. Progress will also depend on the agency priorities and resources. The approach that is outlined in this EHS research strategy document is a stage in the ongoing coordination of the NNI EHS research program. With the rapid development of technology and information on effects related to human and environmental exposure to nanomaterials, the NEHI Working Group will update the strategy to keep the NNI focused on top EHS research priorities and to ensure sound risk management of engineered nanoscale materials into the future.

Table 1. Priority Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials

Instrumentation, Metrology, and Analytical Methods

1. Develop methods to detect nanomaterials in biological matrices, the environment, and the workplace
2. Understand how chemical and physical modifications affect the properties of nanomaterials
3. Develop methods for standardizing assessment of particle size, size distribution, shape, structure, and surface area
4. Develop certified reference materials for chemical and physical characterization of nanomaterials
5. Develop methods to characterize a nanomaterial's spatio-chemical composition, purity, and heterogeneity

Nanomaterials and Human Health

Overarching Research Priority: Understand generalizable characteristics of nanomaterials in relation to toxicity in biological systems.

Broad Research Needs:

- Understand the absorption and transport of nanomaterials throughout the human body
- Develop methods to quantify and characterize exposure to nanomaterials and characterize nanomaterials in biological matrices
- Identify or develop appropriate *in vitro* and *in vivo* assays/models to predict *in vivo* human responses to nanomaterials exposure
- Understand the relationship between the properties of nanomaterials and uptake via the respiratory or digestive tracts or through the eyes or skin, and assess body burden
- Determine the mechanisms of interaction between nanomaterials and the body at the molecular, cellular, and tissular levels

Nanomaterials and the Environment

1. Understand the effects of engineered nanomaterials in individuals of a species and the applicability of testing schemes to measure effects
2. Understand environmental exposures through identification of principle sources of exposure and exposure routes
3. Evaluate abiotic and ecosystem-wide effects
4. Determine factors affecting the environmental transport of nanomaterials
5. Understand the transformation of nanomaterials under different environmental conditions

Human and Environmental Exposure Assessment

1. Characterize exposures among workers
2. Identify population groups and environments exposed to engineered nanoscale materials
3. Characterize exposure to the general population from industrial processes and industrial and consumer products containing nanomaterials
4. Characterize health of exposed populations and environments
5. Understand workplace processes and factors that determine exposure to nanomaterials

Risk Management Methods

Overarching Research Priority: Evaluate risk management approaches for identifying and addressing risks from nanomaterials

1. Understand and develop best workplace practices, processes, and environmental exposure controls
2. Examine product or material life cycle to inform risk reduction decisions
3. Develop risk characterization information to determine and classify nanomaterials based on physical or chemical properties
4. Develop nanomaterial-use and safety-incident trend information to help focus risk management efforts
5. Develop specific two-way risk communication approaches and materials

II. Summary of NNI EHS Research: Portfolio Review and Gap Analysis

A key step in the process for developing the NNI research strategy for nanotechnology-related EHS research is collecting and assessing data on the NNI agencies' current research activities. As described earlier, the Office of Management and Budget (OMB) asked agencies to provide lists of EHS-related projects that were funded or active in FY 2006 in each of the five research categories outlined in Table 1. The resulting list of projects (both intramural and extramural) is shown in Appendix A. In summary, the data presented in the appendix shows that in FY 2006 the Federal Government invested \$68 million in 246 nanotechnology-related EHS research projects at seven agencies. Although research categories were not prioritized with respect to each other, there is consensus among members of the NEHI Working Group that research in the Instrumentation, Metrology, and Analytical Methods category is cross-cutting, supporting research in every other category, and therefore is generally a high priority. Among the five research categories, the distribution of projects and spending was: 78 projects (\$26.6 million) in Instrumentation, Metrology, and Analytical Methods; 100 projects (\$24.1 million) in Nanomaterials and Human Health; 49 projects (\$12.7 million) in Nanomaterials and the Environment; 5 projects (\$1.1 million) in Human and Environmental Exposure Assessment; and 14 projects (\$3.3 million) in Risk Management Methods.

This section includes a summary of the data that were reported in response to the OMB data call, an analysis of that data (i.e., the types of projects that were reported and the relative levels of investment among the various research priorities), and concludes with a discussion of the strengths, weaknesses, and gaps in the current research portfolio. This in turn informs the strategy for future NNI EHS research that is outlined in later sections of this document. This analysis of strengths, weaknesses, and gaps will inform agency decisions about the magnitude and balance of future EHS research investments. The section begins with a brief description of the request made by OMB to the agencies to obtain the data on EHS research and how the resulting data were categorized and analyzed by the NEHI Working Group. It is important to understand that the data gathered for FY 2006 represent a one-time-only "snapshot" of the NNI agencies' EHS research portfolios in one year. However, these are likely to be indicative of the overall trends in agency investments in more recent years.

The bulk of this section provides an in-depth analysis of the current research being conducted in each of the five NNI EHS research categories. For each of the categories, a table is included showing the total estimated funding and number of projects, broken down by the prioritized research needs for that category. The table is followed by an overview of the types of projects included in that research category, then by a summary analysis of the projects reported for each research need under that category, including a discussion of strengths, weaknesses, and gaps. Each research category subsection concludes with two figures:

- (1) A graphical representation of the identified priority research needs, the key research activities to address each need, and the relative emphasis to be given to the research needs and associated key activities as a function of time. Shading is a general indication of the staging of research across the near term (1-5 years), medium term (5-10 years), and longer term (more than ten years). These are intended to account for interdependencies among research efforts while ensuring information is available when needed. The timing of any research project is accompanied by significant uncertainties, particularly when new understanding of fundamental processes is required and the field is as new as this one. New cycles of scientific advancement are stimulated by new scientific understanding and evolving technologies for measuring and monitoring. Progress in several of the priority research needs is contingent upon successful research in others, particularly metrology. Timeframes for those research needs is thus relative to the availability of contingent information. The development of new materials will also reset some of the timeframes for those research needs related to these materials.

- (2) A framework diagram showing how the five research priorities in the respective category correlate with the phases outlined in the overall simplified framework for research related to EHS risk assessment of nanomaterials shown in Figure 2. These framework diagrams also show which phases of the simplified framework are relevant to each of the identified priority research needs for that category.

Data for Fiscal Year 2006 Research

Data to support an evaluation of current research in EHS priority areas and a comparison with previously specified research needs was obtained to identify areas of weakness or gaps. The data were obtained through a data call issued by the Office of Management and Budget (OMB) regarding research for FY 2006 that was relevant to the five EHS research categories (see Appendix A). These data enabled an assessment based on a snapshot of the Federal research investment in one year in an approach that compared the relative balance of funding across the research needs with respect to the priority of those needs. Priority in this case was considered both in terms of the kind of information developed (some information is of greater relevance than others to supporting risk management) and the appropriate sequencing of research (some research should be timed to occur following other research in order to gain the greatest benefit to decision making with respect to product use, regulations, and conduct of research). Projects relevant to more than one category or need were assigned to the need that was primarily being addressed by the research. In a small number of cases, it was not possible to identify a single primary need, and these were categorized as addressing “multiple” needs. In some cases, projects were related to the overarching research category, but did not align with any of the top five priority areas. These projects were categorized as addressing “other” needs.

When analyzing these data and using them for the purposes of a gap analysis with respect to the overarching research needs, the following limitations must be considered:

- The data represent only research funded in FY 2006. Many projects are multiyear and therefore actual research associated with projects listed may have taken place in earlier or later years. Projects begun after FY 2006 are not captured.
- Projects listed are prospective, that is the projects are planned research not research results. Basic research projects may diverge from the original proposals, based on initial results or as other information becomes available.
- The list represents only Federally funded research. It does not include any research in these areas that is supported by industry, nonprofit organizations, or other countries.

Description of Process for Performing Gap Analysis

The gap analysis, identification of prioritized research needs, and “balance-assessment” began via a series of interagency meetings and discussions by nanotechnology EHS experts across Federal Government agencies. *For purposes of this document, balance-assessment refers to the relative allocation of resources among priority research needs within a research category over the course of implementing the NNI EHS research strategy.* The group of experts representing the NEHI Working Group member agencies considered available information from the snapshot of FY 2006 portfolio of nanotechnology-related EHS research obtained by OMB. The group proceeded to examine the projects as they had been assigned by funding agencies to the research categories given in the September 2006 NNI EHS Research Needs document, and took into account overlaps of individual projects across different research categories and priority needs. The experts also reassigned projects between categories and priority needs in some cases. As such, research funded by the NNI agencies was to a degree validated by the experts according to their application to the NNI EHS research categories and research needs of Federal agencies. In addition, the overall application of each project with respect to the development of information that enables both protection and

beneficial applications of nanotechnology for human and environmental health was considered throughout the review process.

The group of experts also considered the ability of research, as captured by the prioritized research needs within each category, to provide results that would address current needs for nanotechnology-related EHS risk management. When such activities were deemed absent, particularly when activities were absent for an entire group of research needs, these areas of research were highlighted as future priorities through a balance-assessment process. Balance-assessment as used here refers to the relative emphasis, and relative allocation of resources, among research needs within a research category. In some cases projects were reported for a priority research need, but the breadth and depth of the projects were insufficient. These were not necessarily considered as gaps, but rather as areas that could be targeted for greater emphasis in the future. Summaries of the FY 2006 project data and an analysis of the data for each of the research categories are provided in the next section.

Within the NSET Subcommittee member agencies and the NEHI Working Group member agencies, nanotechnology-related EHS research planning and project implementation have been taking place simultaneously for several years. The NNI agencies have been funding basic research and technology development and through these activities have been producing information critical to this field. Moreover, the overall analysis of the data call indicates that many of the priority research areas are already receiving considerable support and that ongoing research is strongly aligned with the priority research needs that were identified prior to the OMB data call. NNI agencies have expended EHS resources through avenues other than research, for example, workshops, task forces, white papers, peer reviews, and public meetings. While these more applied efforts are generally not portrayed as research, they are nonetheless essential to furthering progress in nanotechnology-related EHS research and are key elements in the overall Federal EHS portfolio.

Analysis of FY 2006 EHS Research by Five Priority Categories

Research Category: Instrumentation, Metrology, and Analytical Methods

Total estimated funding in FY 2006: \$26.6 million

Total projects: 78

Agencies supporting research in this category: DOE, NIH, NIOSH, NIST, NSF

Prioritized EHS Research Needs for Instrumentation, Metrology, and Analytical Methods	FY 06 funding Estimate \$K (% of total)	Number of Projects (% of total)
1. Develop methods to detect nanomaterials in biological matrices, the environment, and the workplace	12,396 (47%)	36 (46%)
2. Understand how chemical and physical modifications affect the properties of nanomaterials	2,845 (11%)	14 (18%)
3. Develop methods for standardizing assessment of particle size, size distribution, shape, structure, and surface area	2,012 (8%)	4 (5%)
4. Develop certified reference materials for chemical and physical characterization of nanomaterials	4,319 (16%)	6 (8%)
5. Develop methods to characterize a nanomaterial's spatio-chemical composition, purity, and heterogeneity	3650 (14%)	15 (19%)
Multiple: Projects that capture multiple needs	1300 (5%)	2 (3%)
Other: Not captured in needs above, but of benefit to the research category	50 (0.2%)	1 (1%)

Background

The research needs in this research category represent the highest-priority research that is essential to understanding, predicting, and quantifying the chemical and physical properties and behavior of nanomaterials. The priorities underpin, and are fundamental to, all five categories of nanotechnology-related EHS research and information needs. Much of the research also is important for development of nanomaterials for beneficial applications.

Seventy-eight projects were identified as falling under this category of nanotechnology-related EHS research. The majority of the projects focused on priority research need #1 (to detect nanomaterials in biological matrices, the environment, and the workplace); priority research need #2 (to understand how chemical and physical modifications affect the properties of nanomaterials); and priority research need #5 (to characterize a nanomaterial's spatio-chemical composition, purity, and heterogeneity). Work is limited but underway for addressing priority research need #3 (determination of particle size, size distribution, shape, structure, and surface area), with 4 projects. Work on priority research need #4 (to develop reference materials) is reported, and is part of work listed in other categories as well. Only one project in this category fell outside the five priority research needs, indicating that even before the priority research needs were identified, NNI agencies have been focusing on the top priorities for this category.

As there is a low number of projects for determination of particle size, particularly in biological, environmental, and other complex media, efforts could be stronger in this area. The ability to accurately measure particle size is critical because size is increasingly recognized as important to determining potential environmental and human health risks of ambient particulate matter. In addition, the detection of nanomaterials in solid media, such as soil, is not well addressed. This inhibits the ability to monitor and track nanomaterials in the environment or in solid waste streams. Work towards the development of samplers and instruments for monitoring the environment and the workplace has been limited. Reporting of environmental and workplace nanomaterial sampling efforts are appropriately reported in the Nanomaterials and the Environment and in the Nanomaterials and Human Health research categories.

A fundamental requirement for assessing the potential impacts of new nanomaterials on both human health and the environment is the ability to make precise, accurate measurements at the nanoscale in multiple, complex media. Moreover, unique measurement technology challenges must be met, such as investigating how nanomaterials interact with different environments and effects that may occur at various points of nanotechnology-enabled products' life cycles including those that may be due to transformations. As such, research to support the Instrumentation, Metrology, and Analytical Methods category supports all aspects of the Human and Environmental Exposure Assessment category and is overarching to the other four research categories. In particular, the development of methods to detect nanomaterials in biological matrices, the environment, and the workplace is necessary across the entire framework from the synthesis and use of nanomaterials to the detection and characterization of materials as a function of exposure. Similarly, the development of methods for determining the sizes, shapes, structures, and surface areas of nanomaterials are essential to assess such metrics from the beginning phases of material production through the characterization of a material that leads to a dose effect.

At present the characterization of materials at various stages of development, including assessments of biological response, often do not provide measurements that are reproducible or consistent across disciplines and applications. As such, reference material development plays a key role in these areas by providing a standardized, acceptable approach to study, monitor, and potentially track nanomaterials as they are released into the environment or the workplace, and to assess their potential interactions with human and ecological systems. Methods for the determination of the spatial composition, purity, and heterogeneity also play a pivotal role for these areas, because single defects or slight changes to surface dimensions or composition can dramatically influence the nanomaterial life cycle and the biological or environmental effects that may result at any given point. Similarly, methods to support understanding how chemical and physical modifications affect the properties of nanomaterials are critical for

assessing nanomaterials beyond external contact, because modifications may affect the ability of a material to migrate into or travel within both human and environmental contexts.

Summary of Analysis by Research Need

Research Need #1: Develop methods to detect nanomaterials in biological matrices, the environment, and the workplace

Analytical methods for identifying and measuring the critical parameters related to nanomaterials in biological systems, the environment, and the workplace are not well developed or readily available. As a result, these important metrics are infrequently or inaccurately reported. Further development of these methods is critical to all nanotechnology EHS research.

Thirty-six projects are identified for this priority research need. All of the projects support the four other research categories. Several projects are focused on: (a) the development of enhanced microscopic techniques relevant to biological imaging and fluorescence of individual molecules; (b) development of potent magnetic resonance imaging (MRI) contrast agents and probes vital to achieving cellular and molecular imaging with MRI for improved detection capabilities, including a safe and sensitive imaging probe for *in vivo* molecular imaging; and (c) the synthesis of new ceramic nanoprobe for bio-imaging that are highly fluorescent, bio-compatible, and nontoxic. Quantum optical measurement approaches are under development. Also under investigation are issues determining the complete cycle of nanoparticles within biosystems and capabilities to predict how readily nanoparticles may enter tissues and cross membranes. This includes characterization of particle dimensions in two and three dimensions to obtain structural information on nanoparticle shape and size using image-enhancing simulations. This latter work overlaps with research need #5 in this category.

Several projects have specific nanotechnology application foci with an emphasis on the characterization of nanomaterials in tissues, cells, or at subcellular levels. Such studies can provide insight into mechanisms of nanoparticle transport in tissue. Enhanced capabilities for detection of nanomaterials may result from some of these application studies as well. For example, the development of biological or chemical sensors and *in/ex vivo* biomedical diagnostics and therapies may result. To realize such applications it is important to note that fundamental properties do not necessarily scale from macroscale to nanoscale regimes. Therefore, progress toward applications requires developing new quantitative nanoscale metrologies and databases of properties to support these and further investigations (structural, chemical, electronic, optical, transport). The use of nanomaterials for multifunctional sensors and characterization of nanocomposite thin films for device applications is one area of ongoing work that supports this notion, as is work to enable rapid, accurate imaging of thermal and mechanical properties at nanometer length scales to understand and control the thermal and mechanical behavior of materials at the nanoscale. This latter activity targets photoacoustic and photothermal measurement capabilities for the noncontact and nondestructive imaging of surface properties and subsurface defects at the nanoscale, a critical area for detection of nanomaterials.

Development of detection capabilities that can be applied to cellular biophysics, biosensing, nanoscale devices, and translational applications in medicine and environmental sciences is underway. Nanoparticle research on enabling computational and characterization tools with a focus on materials, devices, and the environment also supports such efforts. Innovations in these areas will likely benefit research applications beyond those described and may apply to many aspects of detecting and characterizing nanomaterials in biological and environmental media and possibly the workplace environment.

Research Need #2: Understand how chemical and physical modifications affect the properties of nanomaterials

In the development of products, nanomaterials may undergo any number of modifications, including applications of coatings to reduce oxidation, addition of molecular groups to induce or diminish biological activity, or functionalization to enable integration of materials into final products. Research in this priority research need provides information on how such changes or modifications to nanomaterials may affect their behavior, including their degradation and their uptake by biological materials. Modifications may also affect the chemical and physical properties of nanomaterials and the methods necessary to detect the nanomaterials in human and environmental media.

There are fourteen projects within this priority research need. In particular, interactions at the single-molecule level are under study. Such investigations lead to understanding interactions with complex systems such as molecular aggregates, proteins in biological membranes, or semiconductor nanostructures. The ability to detect a single molecule in a complex environment with a spatial resolution in the order of 10-20 nanometers may be realized. This work largely overlaps with research need #1. Research toward understanding and controlling the chemical properties of reactive metal nanoparticles is also underway; this includes characterization of their surface and bulk composition. Such research on shells or coatings plays a major role in determining reaction pathways. It is noted that relationships of such pathways to toxicity and environmental health are lacking and are essential to understanding how chemical and physical modifications affect the properties of nanomaterials.

Quantitative investigations of the effects of size, surface composition, proximity, and dopants on semiconductor nanoparticle properties are underway. Such work provides insight into methods of particle synthesis that allow control over these parameters. The use of synchrotron-radiation-based characterization methods that provide element-specific atomic and electronic structure information enhances this effort by refining our understanding of quantum dot structure/property relationships. Additional work focused on the diffraction of glasses, liquids, and nano-clusters is providing data on the structure of nano-phase clusters in zeolites in distinct environments to correlate molecular structure with electronic structure of caged semiconductors. Such information provides insight into how modification of nanomaterials, such as changing their environment, affects their properties—a main concern for this priority research need.

New methods and instrumentation for the study of magnetic materials and nanostructures using soft X-ray spectroscopies enables the study of engineering materials for applications as sensors, actuators, and spintronic devices. A theoretical component of this provides support for applying spectroscopies to the problems of complex materials, including understanding chemical and physical modifications. Theory and prediction studies on the chemical properties of nanostructures are also underway. Additional work on magnetic properties includes the use of spin-polarized positron beams for the measurement process. Electron energy loss spectroscopy to determine the physical and mechanical properties of nanoscale materials provides data on mechanical properties such as bulk, shear, and elastic properties. It is very difficult to obtain such property data for nanomaterials by other techniques. Nanoporous alumina tubes have gained significant interest in drug delivery and gas separation technologies. As such, their use as membranes for hemodialysis is under investigation, which includes characterization efforts on porosity and pore size distribution, chemical and thermal degradation, and mechanical properties.

Three projects provide application foci. One provides insight into the processes occurring on or near zero-valent iron surfaces. Techniques designed to probe the surface, such as potentiometry, surface-enhanced Raman spectroscopy, and electrochemical quartz microbalance methods are under investigation. This work strongly overlaps with the Nanomaterials and Environment category. The other two projects that focus on applications overlap with the Nanomaterials and Human Health category. One is focused on bladder tissue engineering through nanotechnology; the other makes use of nanotechnology to develop the basic science of nanoparticle thin films, which could lead to the novel nanotechnology-based sensors for biomaterials with an affinity for gold (i.e., homocysteine, cysteine) and

other functionalized surfaces. Characterization of the nanomaterials, which are modified and engineered for specific applications, support this research need.

Research Need #3: Develop methods for standardizing assessment of particle size, size distribution, shape, structure, and surface area

This research need seeks to provide rapid, statistically valid, standardized methods for measuring particle size, size distribution, shape, structure, and surface area of nanomaterials. Four projects support this research need.

One project includes nanoparticle and nanomaterial metrology research. It is focused on determining particle size and particle size distributions with additional efforts focused on determining shape, structure, and surface area using various techniques. A second project consists of an instrument development project, specifically, the development of a laser-based instrument to measure both particle size and electrostatic charge distributions in real time and on a single-particle basis for particles in the size range 10 to 1000 nanometers. This instrument will support many aspects of the other research categories. A third project provides research to enable development of a comprehensive yet practical method for sampling, quantification, and characterization of carbon nanotube (CNT) particles in air. This method will be capable of classifying sampled particles into categories of carbon nanotubes and measuring for each type the number concentrations, size distributions, and the shape characteristics (diameter, length, aspect ratio, and curvature). A fourth project for this priority research need is an investigation of size-exclusion-based separation techniques. While the study is focused on an application, it may provide information to support the development of nonconventional particle size analyzers.

Since there are only 4 projects for this research need, it appears efforts could be stronger for this area. The fundamental work that is reported is essential to furthering our ability to accurately measure nanoparticle size, size distribution, shape, structure, and surface area. Beneficial enhancements that could augment these efforts include the development of automated microscopic methods for the screening of a large number of nanomaterials, investigations on the correlations of microscopic methods with other methods (such as techniques based on light scattering) and the improvement of size methods for the reproducible determination of particle sizes <5 nanometers. Critical biological (and possibly environmental) processes occur in this size range, and the ability to measure particles at this scale is necessary for accurately assessing nanomaterial EHS aspects. It is noted that one project in the Human and Environmental Exposure Assessment category provides funding for research to identify and evaluate methods to measure airborne nanoparticle concentrations and the development of methods to characterize nanoparticles using a complementary suite of techniques to assess their surface and bulk physical and chemical properties. Two projects in the Nanomaterials and Human Health category also have components supporting the development of methods that meet metrology priority research need #3.

Research Need #4: Develop certified reference materials for chemical and physical characterization of nanomaterials

This research need seeks the development of reference materials for the chemical and physical characterization of nanomaterials. Reference materials are beneficial for calibration of instruments or analytical processes used to assess the chemical or physical properties of nanomaterials. They are also needed to assess the quality or comparability of results from tests or assays designed to determine the toxicity of health-benefit or drug-related materials. Six projects support this research need.

Specific materials under development include carbon nanotubes, nanoparticles that are non-carbon-based such as metal oxides, nanostructured powders, fibers, and engineered tissue substitutes. The latter could be useful for the next generation of natural-matrix frozen tissue materials designed to mimic nanomaterials used for bioengineering and tissue engineering studies. Such materials include polymer hydrogels or materials with nanoparticles embedded within the matrix for functional, stability, or antioxidant capabilities.

While efforts in this area are limited to six projects, the reported work supports a fundamental start for the development of nanoscale reference materials. Efforts could be stronger for the development of materials that are tailored specifically for toxicology and environmental studies, because research on these research topics is limited.

Research Need #5: Develop methods to characterize a nanomaterial's spatio-chemical composition, purity, and heterogeneity

At the nanoscale, single defects and slight changes to surface dimension and composition can dramatically influence reactivity; hence, proper characterization of spatial composition is critical. This research need seeks methods to characterize a nanomaterial's spatial composition, the identification of possible defects or impurities, and batch-to-batch variation in nanomaterial production or biological activity. Fifteen projects support this research need.

Projects provide information on the chemical, energetic, crystallographic, and structural composition of nanomaterials, providing some degree of 3D imaging. Chemical projects range from characterizing reactions at solid/gas and solid/liquid interfaces to probing details of heterogeneous chemical reactions and of chromatographic processes. Atomic-scale 3D chemical imaging of interfaces in nanostructures uses a combination of electron tomography, energy-filtered transmission electron microscopy, and aberration correction. Aberration correction may improve the resolution in energy-filtered imaging to the atomic level. Currently such imaging is limited to approximately 1 nanometer for many applications. This combination improves resolution, sensitivity, and validity of data interpretation beyond what is typically available.

The study of energy interactions with surfaces provides a basis for modifying, patterning, and analyzing surfaces and nanoscale properties of materials. Mass-based analysis of materials with nanometer scale lengths may be realized. Studies are underway that are focused on property-sensitive nanoscale structure and defects. These studies use quantitative electron microscopy techniques, such as coherent diffraction, atomic imaging, column-by-column spectroscopy, and phase retrieval methods, including electron holography, in combination with simulations and theoretical modeling.

The expert analysis of the projects in this research need noted the development of a wide range of microscopic and spectroscopic techniques applicable to a broad range of nanomaterials. These likely can be implemented in many existing research facilities. In addition, two specific application projects support this research need. The first uses a powder X-ray diffractometer for environmental, materials science, and chemical research. The second application project employs extreme UV in a variety of applications to efforts such as high-resolution imaging, spectroscopy, elemental- and bio-microscopy, and nanofabrication. Topical areas for these projects overlap with the Nanomaterials and Environment category, for example chemistry and mobility of contaminants.

Projects in this research need overlap with research need #1, the development of methods to detect nanomaterials in biological matrices, the environment, and the workplace. Stronger efforts should be devoted to imaging of nanomaterials in biological media with an emphasis on the co-determination of a material's spatio-chemical composition, purity, and heterogeneity. Such work would greatly assist nano-EHS studies, because the determination of these metrics is essential to understanding toxicological effects of nanomaterials.

Projects Classified as “Multiple” or “Other”

Two projects are placed in the “multiple” category, because it appears that multiple priority needs are being met via activities on characterization of nanomaterials and the development of tools, techniques, and Internet and computational infrastructure development. One additional project is placed in the “other” category, because this is targeted to using nanostructured thin films for improving the performance of sorbents used in gas chromatography, with applications in homeland security, monitoring food freshness, industrial process control, biomedical diagnostics, and surveying environment quality. This is an application of nanomaterials for improving measurements in environmental and occupational safety, but it is not captured in the five priority research needs.

Summary of Balance-Assessment for Instrumentation, Metrology, and Analytical Methods Category

There is fundamental, solid research activity in this category. Much of the research reported for FY 2006 is focused on the development of either adapted or new technologies to measure the amount or type of nanomaterial in a given space or time: these efforts contribute substantially to the overall ability to understand and manage potential risks of engineered nanomaterials. Mechanistic studies of broad classes of nanomaterials are underway. Integration of these across media that are indicative of exposure would enhance nanomaterial health and safety research and as such, should be a near-term focus for the development of methods, as detailed in Figure 3, where relative timing of research needs is indicated. In addition, universal air samplers are not available; therefore, research to develop such instruments should begin right away. Also needed in the near term are evaluations of nanomaterials with respect to solubility in lipids and aqueous environments, in order to assess nanomaterial correlations with transport phenomena across membranes or in aqueous environments. Such activity would provide datasets for risk assessment and management that can build upon existing research whose primary focus is predictive toxicology or environmental modeling.

Mid-term efforts should focus on technology developments for the monitoring of nanomaterials in water. This technology would then support studies on understanding the effect of surface function on the behavior of nanomaterials in water, one of the research topics under priority research need #1 in Figure 3. Reference materials developed for these types of studies in the mid term would also greatly facilitate such investigations and provide a basis to build modeling platforms to predict environmental behavior of nanomaterials—a longer-term research activity not present on the agenda but one with existing activity that can be built upon.

Explanation of Research Emphasis Diagrams

Based on the analysis of the range of needs in the research need categories, research emphasis diagrams have been developed to show the relative time frames and sequences in which the task forces felt the research to address the five research needs within each category should take place. The timing of each area depends on the immediacy of the need for the results and whether other research or information is needed before the subject research can be undertaken. Color shades correlate with relative level of emphasis (i.e., darker shades represent greater emphasis). Changes in relative level of emphasis through time in a given research area will presumably correlate with variation in level of spending. However, the color shades do not indicate levels of funding relative to other research categories or research needs. The estimated time required to carry out a particular area of research will depend to some extent on the level of funding and, in some cases, on progress in related areas of research. Therefore, the starting time and the duration of high-intensity activity shown in this and other diagrams in this section are estimates and may be subject to modification.

Figure 3. Relative emphasis as a function of time for EHS priority research needs: Instrumentation, Metrology, and Analytical Methods category

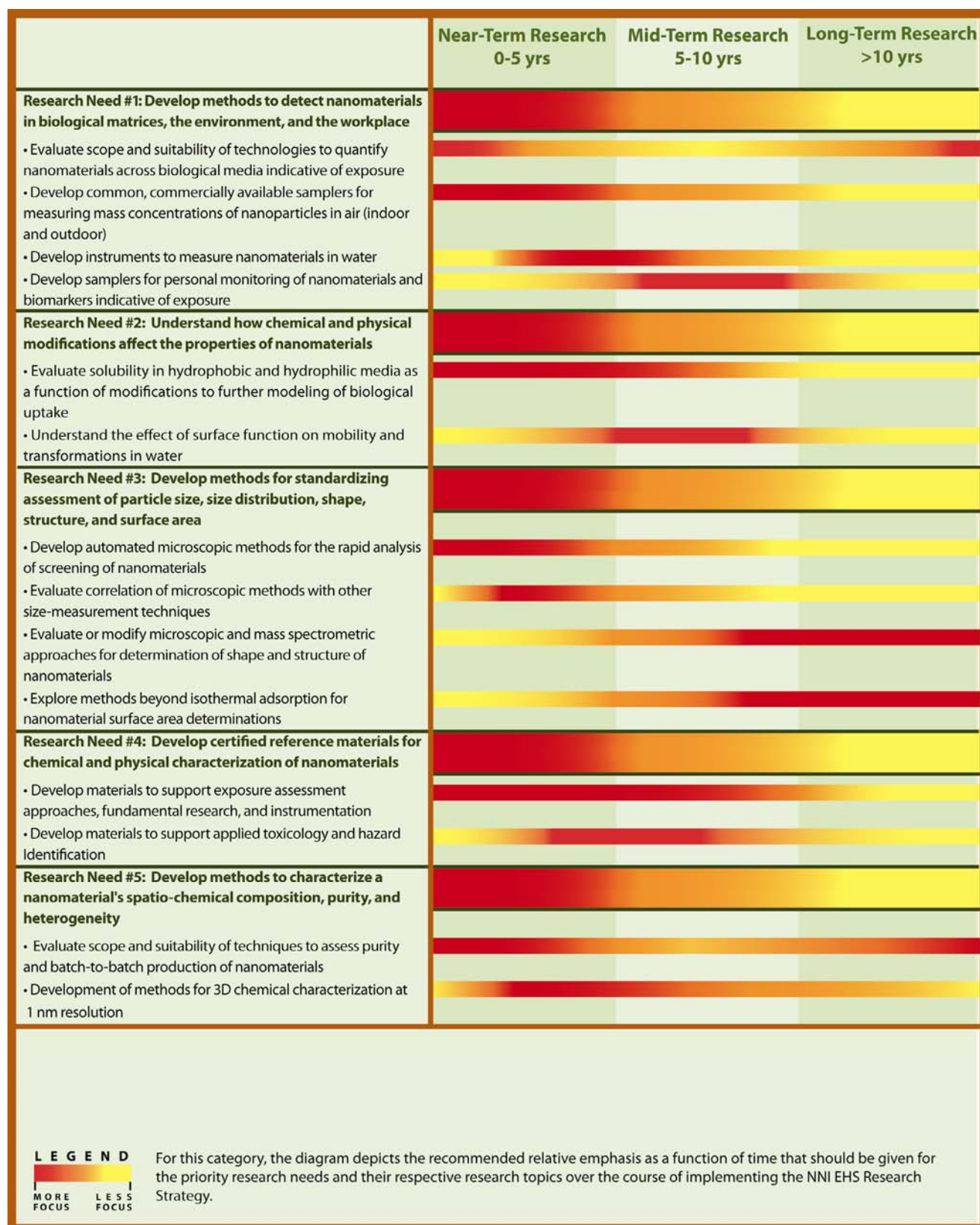
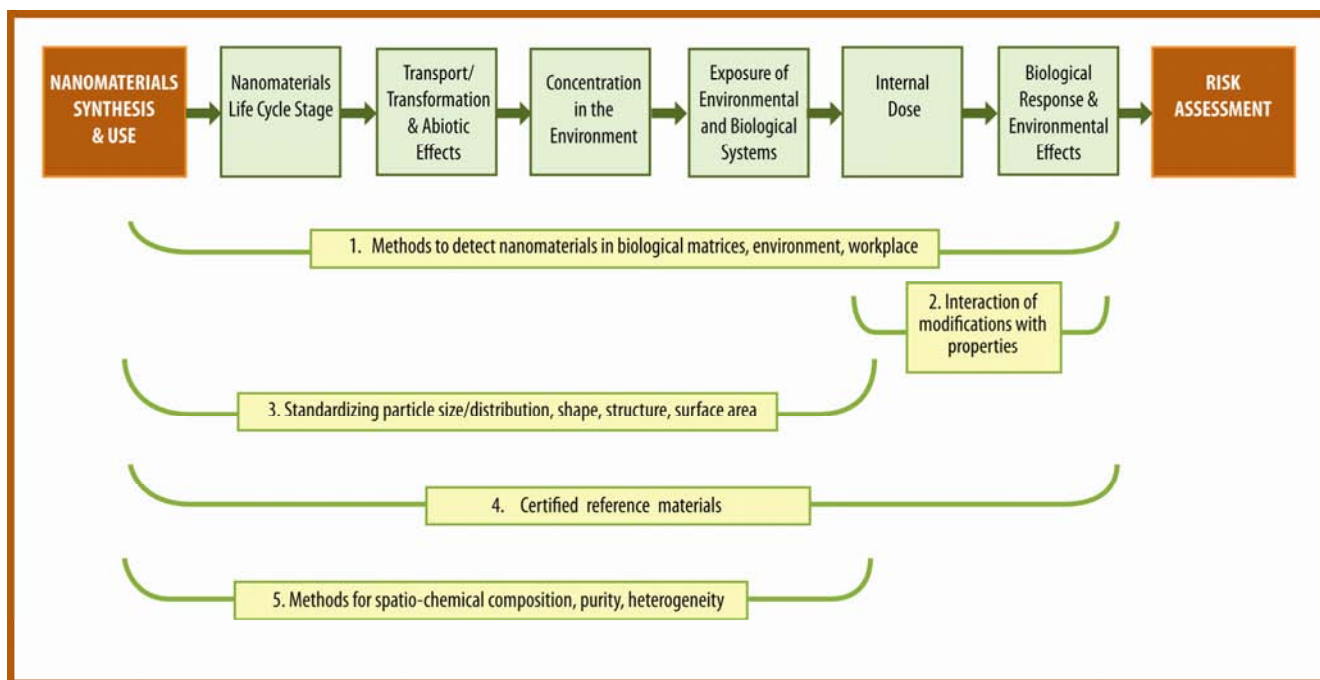


Figure 4. Framework for EHS research on Instrumentation, Metrology, and Analytical Methods*



* This diagram is not comprehensive and is only intended to qualitatively show the general relationships between the prioritized research needs within this category and phases of the simplified framework for research related to EHS and risk assessment of nanomaterials shown in Figure 2. The sizes of the boxes for the prioritized research needs are not intended to imply any differences in degree of emphasis or level of effort. The green lines extending outside the boxes indicate roughly the phases of the simplified framework that are to be addressed by each of the identified priority research needs of this category.

Figure 4 represents the conceptual framework for the relationship between Instrumentation, Metrology, and Analytical Methods research needs and the sequence of events for decision making with respect to nanomaterial use. A fundamental requirement for assessing the potential impacts of new nanomaterials on both human health and the environment is the ability to make precise, accurate measurements at the nanoscale in multiple, complex media. Moreover, unique measurement technology challenges must be met, such as investigating how nanomaterials interact with different environments and effects that may occur at various points of the nanotechnology-enabled products' life cycles, including those effects that may be due to transformations. As such, research to support the Instrumentation, Metrology, and Analytical Methods category covers all aspects of the Human and Environmental Exposure Assessment category and provides a foundation for work in the other four research categories. In particular, it is necessary to develop methods to detect nanomaterials in biological matrices, the environment, and the workplace across the entire framework of nanotechnology research, from the synthesis and use of nanomaterials to the detection and characterization of materials as a function of exposure. Similarly, the development of methods for determining the sizes, shapes, structure, and surface area of nanomaterials is essential to assess such metrics, from the beginning phases of material production through the characterization of a material that leads to a dose effect. In addition, the characterization of materials at various stages of development often does not provide measurements that are reproducible or consistent across disciplines and applications, including assessments of biological response. Hence, reference material development plays a key role in these areas by providing a standardized, acceptable approach to study, monitor, and potentially track nanomaterials as they are released into the environment or the workplace, and to assess their potential interactions with human and ecological systems. Methods for determining their spatial composition, purity, and heterogeneity also play a pivotal role, because single defects or slight changes to

surface dimensions or composition can dramatically influence the nanomaterial life cycle and the biological or environmental effects that may result at any given point. Similarly, methods to support understanding how chemical and physical modifications affect the properties of nanomaterials are critical for assessing nanomaterials beyond external contact, because modifications may affect the ability of a material to migrate into or travel within both human and environmental contexts.

Research Category: Nanomaterials and Human Health

Total estimated funding in FY 2006: \$24.1 million

Total projects: 100

Agencies supporting research in this category: DOD/AF, EPA, NIH, NIOSH, NSF, USDA

Prioritized EHS Research Needs for Nanomaterials and Human Health Overarching Research Priority: Understand generalizable characteristics of nanomaterials in relation to toxicity in biological systems	FY 06 funding Estimate \$K (% of total)	Number of Projects (% of total)
• Understand the absorption and transport of nanomaterials throughout the human body	7,758 (32%)	30 (30%)
• Develop methods to quantify and characterize exposure to nanomaterials and characterize nanomaterials in biological matrices	2,985 (12%)	13 (13%)
• Identify or develop appropriate <i>in vitro</i> and <i>in vivo</i> assays/models to predict <i>in vivo</i> human responses to nanomaterials exposure	975 (4%)	6 (6%)
• Understand the relationship between the properties of nanomaterials and uptake via the respiratory or digestive tracts or through the eyes or skin, and assess body burden	2,722 (11%)	11 (11%)
• Determine the mechanisms of interaction between nanomaterials and the body at the molecular, cellular, and tissular levels	9,590 (40%)	39 (39%)
Multiple: Projects that capture multiple needs	--	--
Other: Not captured in needs above, but of benefit to the research category	35 (-0%)	1 (1%)

Background

The five research needs outlined above are critical to addressing the overarching priority to understand generalizable characteristics of nanomaterials in relation to toxicity in biological systems and address critical research steps in the framework. They are essential for the development of computational models that can predict toxicity of nanomaterials and for risk management.

Research on human health often involves complex, interrelated scientific concepts that are investigated most efficiently by a parallel, rather than serial, research paradigm. This parallel structure permits the investigation of single or integrated research questions and the leveraging of progress in related areas. In this analysis, projects may have research components in more than one research need but they are discussed under the research need that describes the primary focus. These broad research needs were considered equally critical to achieving the overarching goal of understanding the potential for human biological responses to engineered nanomaterials.

Summary of Analysis by Research Need

Research Need: Understand the absorption and transport of nanomaterials throughout the human body

Work in this priority research need focuses on absorption of nanomaterials within the exposure organ, translocation out of the exposure organ, and transport through the body. This research also focuses on the uptake of nanomaterials by exposure organs and by cells. There are 30 projects in this research need, 17 that directly address this research need and 13 that have a relevant research component.

Several projects examine the physical and chemical characteristics of engineered nanomaterials that govern their absorption through human routes of exposure, for example, the respiratory tract and skin. The grant evaluating absorption and transport through the skin is designed to establish a structure-permeability relationship between nanoparticles and skin, and to develop quantitative methods to assess this relationship. Other projects are examining the transport and deposition properties of nanoparticles and agglomerates in the lung as a function of mobility-equivalent diameter of the nanomaterial.

Research on cellular uptake of nanomaterials draws heavily, but not exclusively, on experimental and *in silico* biomedical research that designs nanomaterials for improved drug delivery and imaging. Projects in this area are investigating the physical and chemical properties of nanomaterials that enhance or impede transport through the blood and through tissues, cellular uptake, and transport through the intracellular compartments and cytoplasm. The role of the protein coating in transport and uptake is also under investigation. Projects in this research need will provide information on the interaction of nanoparticles with the cell membrane, and will identify mechanisms of transport through the body and the molecular mechanisms by which cells take up nanoparticles. Studies are also testing the intracellular and extracellular forces that stabilize/destabilize micellar nanoparticles, and the properties of nanomaterials that allow them to coexist benignly with the immune system and the reticulo-endothelial system.

Further research on gastrointestinal and intraocular uptake is needed.

Research Need: Develop methods to quantify and characterize exposure to nanomaterials and characterize nanomaterials in biological matrices

Research in this priority research need focuses on methods to quantify and characterize nanomaterials in external and internal microenvironments. There are 13 projects, 12 of which directly address this research need.

The ability to characterize nanomaterials *in vivo* is critical to evaluating toxicity in the dose-response paradigm. Additionally, several studies have indicated that, at the nanoscale, it may not be sufficient to report only mass measurement of the materials used in an experiment and that additional physical and chemical parameters will be needed to understand the biological behavior of nanomaterials.

Projects that identify the second research need listed above as the primary focus of the grant are evaluating multiple methods to characterize nanomaterials. New methods are being developed, such as cell probe force microscopy, which measures directly the interaction forces between nanostructures and living cells, and intracellular microscopy techniques to localize and quantitate nanomaterials deposition, especially in the nucleus. Lung dosimetry models are being used to understand nanoparticle exposure-deposition relationships.

Methods to characterize nanomaterials in biological systems are used to varying degrees throughout all five research needs in the Nanomaterials and Human Health category. Several projects are evaluating additional metrics of dose, including surface area, shape, surface charge, and surface reactivity. Additional research noted in this section includes characterization of lipids with carbon nanotubes, of nuclear delivery of biomolecular-nanogold complexes, of nanostructured membranes with the intestinal tract, and of the pharmacokinetics of nanoemulsions.

Respiratory tract, skin, and intravenous injection are the most studied routes of exposure; gastrointestinal and intraocular uptakes have been less studied. Methods to characterize and quantify nanomaterials in biological matrices will need further development. Methods to quantify and characterize the exposure before uptake by the body is part of the metrology research program and covered in that section.

Research Need: Identify or develop appropriate *in vitro* and *in vivo* assays/models to predict *in vivo* human responses to nanomaterials exposure

There are 6 projects identified under this priority research need, and all directly address this need.

The ability to manipulate easily the surface chemistry of nanomaterials and the almost infinite number of possible permutations makes rapid, relevant, and accurate assessment of the potential toxicity of nanomaterials an important research need. Additionally, the unique properties that emerge at the nanoscale suggest that the validity of existing test methods should be verified.

Two projects address rapid, high-throughput screening directly by employing the well-established zebra fish model or rapid screening of the oxidative stress response. Both systems employ a three-tiered approach in which a significant response in tier 1 leads to tier 2 testing and, as necessary, tier 3. A third project is developing a technique to assess cell and genetic alterations in human and animal cells using chromosomal breaks and the molecules of xenobiotic metabolism and DNA repair.

The additional projects under this research need are developing tests to measure photophysical properties, dispersity, size dimension, and biolocalization by neutron activation analysis, atomic absorption, and radiochemical analysis to accurately estimate nanoparticle concentration in tissues and biological fluids. Others are developing imaging nanoprobe for PET and MRI that will improve localization in tissues.

While there is a low number of projects in this priority research need, this assessment does not capture applicable research in other areas or many additional research efforts on testing schemes that were not captured by the gap analysis, so a determination of future priorities based on this analysis may be misleading.

Research Need: Understand the relationship between the properties of nanomaterials and uptake via the respiratory or digestive tracts or through the eyes or skin, and assess body burden

There are 11 projects identified under this priority research need, 7 of which have this research need as a primary focus.

Projects under this research need use animal models to consider skin, lung, and oral exposure to nanoparticles and evaluate the standard physical and chemical characteristics of the materials, e.g., size, shape, charge, surface area, and solubility. The skin projects evaluate skin penetration and biological response to nanoparticles that enter the skin. Projects employing inhalation methods examine the dose-response relationship for the lung and the heart and translocation of materials out of the lung. They also investigate the deposition and location of the translocated nanomaterials.

The effects of nanomaterials exposure on disease exacerbation are considered for chronic obstructive pulmonary disease and asthma. An asthma grant employs environmental nanomaterials in air pollution. Data are also derived from biomedical studies on pharmacology and biodistribution of nanoscale drug delivery systems, one using oral delivery. This application evaluates therapeutic efficacy and not uptake by the GI tract directly.

Measurements of total body burden are not clearly described in any grant, and no ocular assessment is noted.

Research Need: Determine the mechanisms of interaction between nanomaterials and the body at the molecular, cellular, and tissular levels

There are 39 projects identified under this priority research need, all of which contribute to progress in this area.

The relationship of exposure to human health response is mirrored in the relationship of dose to biological response. Both dose-response and structure-activity relationships are critical to our understanding of the physical and chemical properties of nanomaterials that support safety and efficacy and minimize adverse effects. This research need extends and integrates the first three research needs listed above.

Multiple projects within this priority research need systematically assess the *in vitro* biological response at the molecular level by investigating the effect of such parameters as size, functional group density, structure, polyethylene glycol coating, and synthesis by-products (especially heavy metals such as iron) on cellular and organ system function. Critical questions being addressed include interaction of nanomaterials with lipids in the cell membrane, proteins, and DNA; mechanisms for cellular uptake of nanomaterials; disposition of materials once they are in the cell; and cell function, proliferation, and differentiation.

Monitoring of biological pathways that are linked to disease provides an opportunity to identify the physical and chemical properties that may not support safe design and development. Many of these projects include *in vitro* experiments and *in vivo* animal studies. Several projects are investigating whether or not nanomaterials stimulate an immune response, induce cell death through oxidative stress pathways, promote respiratory and cardiovascular disease, or disrupt DNA and cause cancer. Most applications study the effects of acute exposure, but several address chronic exposure. Within this chronic exposure category, a number of biomedical projects are evaluating the biocompatibility and biodegradation of nanostructured implants for soft tissue and bone repair.

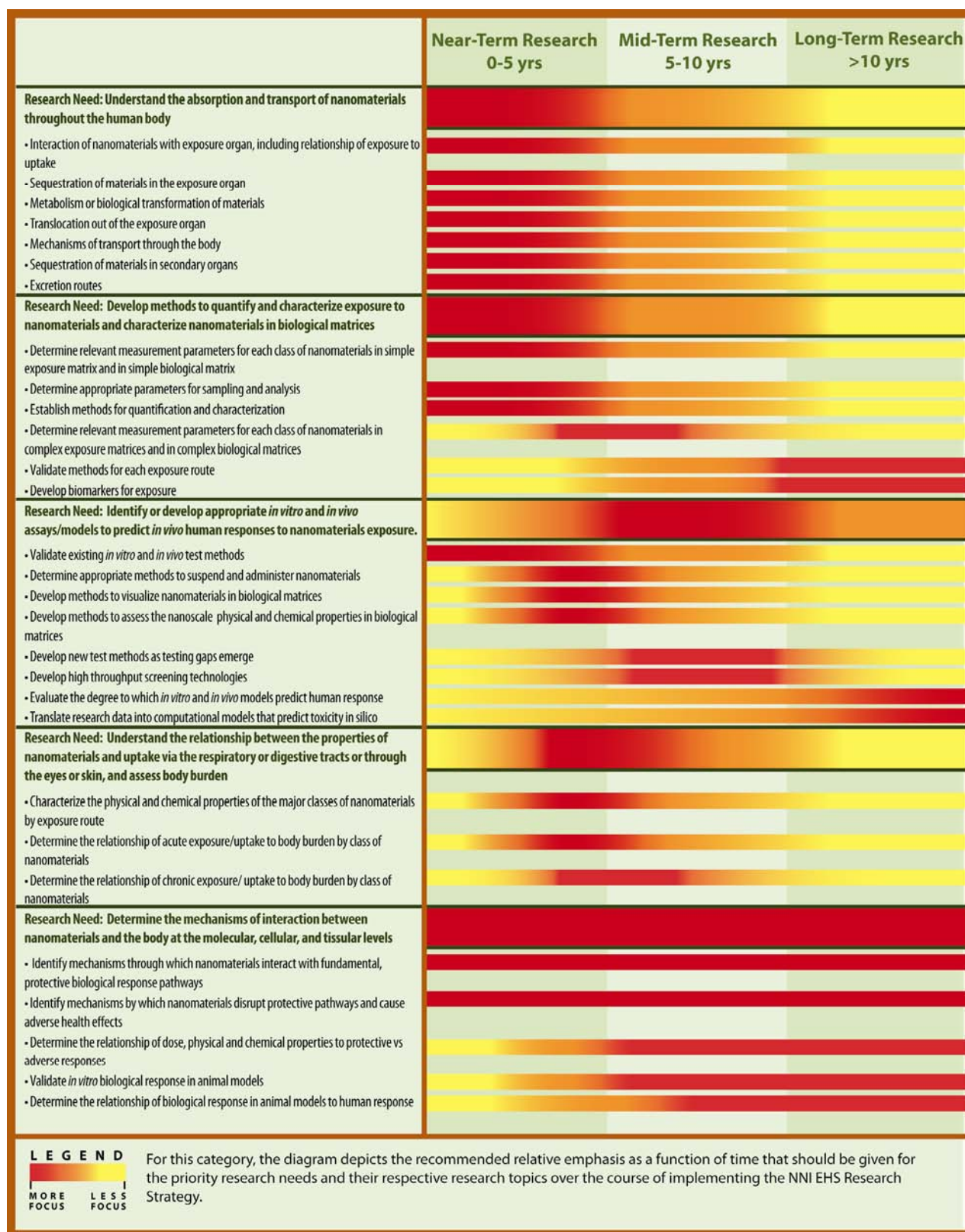
Several projects include the development of computational models. These projects would use the experimental dose-response data to develop models that could predict the potential safety or hazard of new nanomaterials.

The projects reported here encompass the multiple aspects of this research need. It is anticipated that, as research progresses, additional projects will be needed to cover completely the landscape of nano-bio interactions. Additionally, most of the projects employ *in vitro* cellular studies, and there is a need to more fully translate *in vitro* results to animal models and extrapolate data to human exposures.

Projects Classified as “Other”

One project was placed in the “other” research need for this category by the funding agency. This project coordinates research activities on nanoparticles in the workplace.

Figure 5. Relative emphasis as a function of time for EHS priority research needs: Nanomaterials and Human Health category



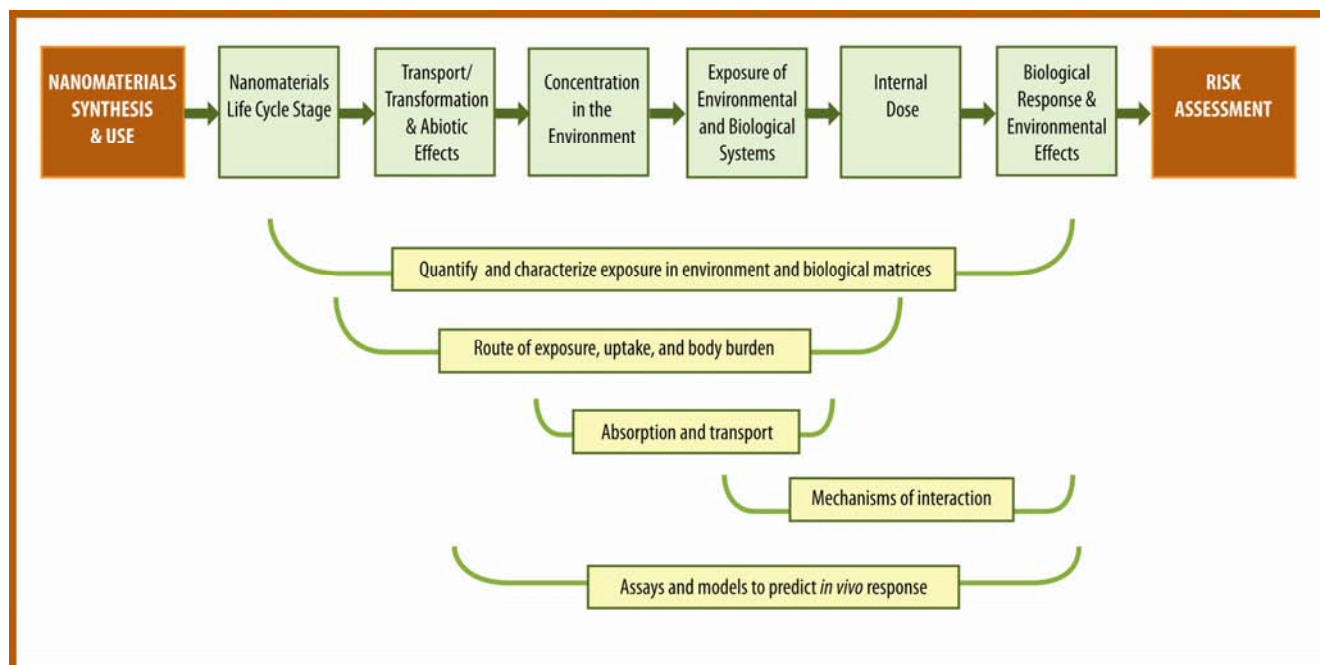
Summary of Balance-Assessment for Nanomaterials and Human Health Category

In FY 2006 projects, there is solid research activity in all five priority research needs for this Nanomaterials and Human Health category, with some weakness observed for gastrointestinal and ocular uptake as well as for the validation of *in vitro* and *in vivo* test methods. Much of the research reported for FY 2006 focuses on medical applications. While this focus does contribute to the overall body of knowledge for human health effects, more systematic, targeted study of classes of nanomaterials and the relationship of their physical and chemical properties to biological response would provide better integrated data sets for risk assessment and risk management. These efforts should build upon the existing research whose primary focus is human health and safety.

Near-term efforts should focus on the research that develops or validates methods to quantify the dose-response, or structure-activity relationships. These efforts should include determining relevant measurement parameters for each class of nanomaterials in simple exposure matrices and in simple biological matrices; the appropriate parameters for sampling and analysis; and methods for quantification and characterization. Methods to quantify and characterize biological response are also critical to dose-response studies and should be developed in the near term.

Mid-term efforts should focus on the application and extension of these methods, as detailed in Figure 5. Missing from the mid-term research agenda is the initiation of an informatics structure to collect, curate, and annotate research data. This mid-term research would support the development of computational models in the long term. In order to advance hazard identification and risk assessment, additional long-term research efforts should translate research findings from animal models to humans.

Figure 6 presents a conceptual framework for the relationship between Nanomaterials and Human Health research needs and the broader context of research supporting nanomaterials risk assessment. The dose-response relationship provides traditional hazard information on the biological response to an exposure. This is one among several relationships that are shown in Figure 6 as a series of related research steps, each of which provides a discrete set of information that, taken as a whole, provides a comprehensive hazard assessment. Steps within the dose component include measurement and characterization of exposure, route of contact with the materials, and internalization of some percentage of the exposure. The response component is comprised of research that includes biotransformation of the material; distribution throughout the system; excretion from the system; and interaction at the cellular, molecular, and organ system level. Because biological response may be dependent on the genetic makeup of the individual, age, health status, gender, socio-economic status, and multiple other life factors, susceptible populations should be included in the framework to designate these considerations.

Figure 6. Framework for EHS research supporting Nanomaterials and Human Health*

* This diagram is not comprehensive and is only intended to qualitatively show the general relationships between the prioritized research needs within this category and phases of the simplified framework for research related to EHS and risk assessment of nanomaterials shown in Figure 2. The sizes of the boxes for the prioritized research needs are not intended to imply any differences in degree of emphasis or level of effort. The green lines extending outside the boxes indicate roughly the phases of the simplified framework that are to be addressed by each of the identified priority research needs of this category.

Research Category: Nanomaterials and the Environment

Total estimated funding in FY 2006: \$12.7 million

Total projects: 49

Agencies supporting research in this category: DOD/AF, DOE, EPA, NSF, USDA

Prioritized EHS Research Needs for Nanomaterials and the Environment	FY 06 funding Estimate \$K (% of total)	Number of Projects (% of total)
1. Understand the effects of engineered nanomaterials in individuals of a species, and applicability of testing schemes to measure effects	1,351 (11%)	5 (10%)
2. Understand environmental exposures through identification of principle sources of exposure and exposure routes	250 (2%)	1 (2%)
3. Evaluate abiotic and ecosystem-wide effects	115 (1%)	1 (2%)
4. Determine factors affecting the environmental transport of nanomaterials	4,490 (29%)	22 (45%)
5. Understand the transformation of nanomaterials under different environmental conditions	2,433 (18%)	9 (18%)
Multiple: Projects that capture multiple needs	--	--
Other: Not captured in needs above, but of benefit to the research category	4,089 (39%)	11 (22%)

Background

Research in this category consists of the five nanotechnology-related EHS research needs, in ranked priority order relative to their importance for the evaluation of potential environmental impacts (see August 2007 Interim EHS Research Priorities document). The first research need comprises research necessary for determining the adverse effects in individuals of both aquatic and terrestrial species and for evaluating the applicability of testing protocols, and associated testing schemes to determine such effects. Consideration should be given to measuring toxicity, mechanisms such as metabolism, and the development of structure-activity relationships.

The second research need is to identify sources of nanomaterials and their routes to the environment, which should provide insights into which environmental receptors, such as individual species, are exposed. Work in this area also includes research to assess the extent to which nanomaterials bioaccumulate in those receptors and identifies relationships between environmental exposure and the absorbed doses in relevant receptors.

The third research need is to determine effects of nanomaterials beyond those in individuals of a species, including those exhibited at the population, community, and ecosystem level, such as alterations to nutrient cycling. This need also includes the study of effects of nanomaterials on other abiotic processes in the environment, such as changes to air quality or photo-oxidative or catalytic effects.

The fourth research need, to determine the factors that affect the transport of nanomaterials in the environment, includes research to understand and predict the transport within and between all environmental media, as well as studies to gain a better understanding of the effects of nanomaterials on the transport and partitioning of other environmental chemicals such as metals.

The fifth research need focuses on examination of transformations of nanomaterials under different environmental conditions, for example, alterations of a material due to changes in groundwater pH or exposure to sunlight.

Research to address all five of the needs in this category should consider not only the parent nanomaterial but also the environmentally altered forms and any by-products caused by reactions, either physical or chemical, of nanomaterials with environmental chemicals or matrices.

Summary of Analysis by Research Need

Research Need #1: Understand the effects of engineered nanomaterials in individuals of a species, and applicability of testing schemes to measure effects

There are five projects identified under this priority research need. Projects on effects of engineered nanomaterials in individuals of a species and on the applicability of testing schemes represent broad coverage of endpoints and species for aquatic receptors. Most of the projects directly address, at least in part, effects in individuals of several species that are included in current test guidelines, including freshwater and marine vertebrates, both benthic and pelagic, and a range of both metallic and carbon-based nanomaterials. Taken together, the projects include a broad range of endpoints from genomic, molecular, and cellular to whole organisms and population-level effects. These projects also include aspects of nanomaterial kinetics, uptake processes, bioavailability, and food chain transfer. Four manufactured nanomaterial classes (metals, nanoceramics, carbon-based nanoparticles, and organic nanomaterials) were addressed by the five projects. (Quantum dots were not addressed.) Additionally, at least three projects from the Nanomaterials and Human Health category will also contribute to the research needs identified here. Terrestrial effects, test protocol development, dose-response characterization, and testing scheme development are less well represented.

Research Need #2: Understand environmental exposures through identification of principle sources of exposure and exposure routes

There is one project identified under this priority research need which focuses on the principle sources of environmental exposures and exposure routes. This work appears to be on naturally occurring nanoparticle effects in geologic systems. This research could be augmented by appropriate research projects in other categories, including those under the Risk Management Methods and the Human and Environmental Exposure Assessment categories that provide sources and routes of exposure from the work environment to broader environmental media. Research will inform which receptors may be of greater concern to examine for effects under research needs #1 and #3.

Research Need #3: Evaluate abiotic and ecosystem-wide effects

There is also one project identified under this priority research need, to investigate effects beyond those in individuals of a species (including abiotic effects). The project addresses natural nanoparticles and their effects on the biogeochemical cycling of metals of concern in the subsurface. Other projects also contribute to an understanding of the effects of nanoscale engineered iron on microbial toxicity, and other higher-level effects, in the subsurface. Coverage of broader nanomaterial classes and effects beyond those seen in the subsurface are not provided. Much of the higher-level ecosystem effects work under this research area will be better focused once information from research needs #1, #2, #4, and #5 are obtained.

Research Need #4: Determine factors affecting the environmental transport of nanomaterials

There are 22 projects identified under this priority research need, to investigate factors affecting the environmental transport of nanomaterials, which touch on all four engineered nanomaterial classes (metals, nanoceramics, carbon-based nanoparticles, and organics), with more emphasis on iron-based particles, and natural nanoparticles, and are funded by five agencies. The transport of nanomaterials in many relevant environmental media is addressed, including soils, the subsurface, surface waters, and wastewater. A significant portion of the research described focuses on the fundamental chemistry and physical properties of nanoparticles that may contribute to the behavior of nanoparticles in the environment (such as formation, stability, media-nanoparticle interactions): such basic information is fundamental to understanding the environmental transport (and transformation) of nanomaterials. However, there is a lack of emphasis in more applied areas related to risk assessment such as determining which physical/chemical processes control the fate and transport of different engineered nanomaterials in environmental media, which in turn would lead to an improved understanding of the key transport processes for commercial nanoparticles. Also, there is a lack of emphasis on the evaluation of traditional existing models and tools to determine their adequacy for predicting nanomaterial transport.

Research Need #5: Understand the transformation of nanomaterials under different environmental conditions

There are 9 projects identified under this priority research need. These projects focus on investigating the physical, chemical, and biological transformations of nanomaterials in the various environmental media, and are funded by four agencies. The research includes representatives of each manufactured nanoparticle class (indicated under research need #4) and selected naturally occurring or incidental nanoparticles. A number of important environmental (soil, sediment, air, and water) and biological matrices are addressed, with an emphasis on varied aquatic media. The research includes attention to environmentally altered forms of nanoparticles, and by-products of reactions between nanomaterials and environmental chemicals/matrices. A number of transformation processes are examined, including coagulation, microbial effects, pH, sorption, and the interactions with specific biomolecules. There is a strong emphasis on fundamental chemical/physical interaction research that will inform transformation processes. In this sense, work described here is similar to that done under research need #4, and many studies under these two priority research needs address topics in both priorities and are mutually supportive. The current state of the science in each of these two priority research needs is at an early stage, such that the focus on fundamental work

is understandable. There is limited work described for biological transformation processes; and there is a need to move toward a focus on key physical, chemical, and biological processes that would be broadly predictive of transformations of manufactured nanomaterials.

Projects Classified as “Other”

There are ten projects that are not captured in the five priority research needs. While these projects do not directly answer questions posed by the five priority research needs, they are useful in the sense that they lead to fundamental understanding of nanoparticle behavior. They also may lead to nanotechnology applications that contribute to lessening current environmental contamination resulting from manufacturing/use/disposal of conventional chemicals.

Summary of Balance-Assessment for Nanomaterials and the Environment Category

The research gaps discussed in the preceding section have been considered, along with additional information, to determine which gaps should be pursued as future research needs. The highest-priority research needs for this category are the same as the first two priority research needs identified earlier in the August 2007 Interim EHS Research Priorities document. However, when assessing the relative priorities of the other three research needs listed in the Interim EHS Research Priorities document for the future, there are four overarching considerations that must be taken into account: (1) a fundamental enabler of work under this research category is the physical/chemical characterization research that enables identification of nanomaterials in biological and environmental matrices; (2) research should focus on the as-manufactured nanomaterial; (3) research should address key products of reactions between nanomaterials and the environment following contact with environmental matrices; and (4) work under this research category will be iterative in nature as new nanomaterial classes come closer to commercial production. The result of this analysis is that for the Nanomaterials and the Environment category, the ranking of priorities was changed from that of the Interim EHS Research Priorities document to that given in Figure 7 and discussed below.

For priority research need #1, work is needed to better understand the potential adverse effects of nanomaterials to biological receptors prior to their commercialization, for developing test protocols for commercial submissions for Federal consideration/approval, developing better understanding of dose-response characterization, and development of tiered testing schemes that incorporate the testing protocols for commercial submissions. This research is considered of highest priority due to: (1) the need to better understand potential impacts on receptors prior to their commercialization, (2) the limited amount of research conducted in this area to date, (3) its achievability in the near term, and (4) its generally high ranking across representative agencies in the August 2007 Interim EHS Research Priorities document. In the near term, test protocol research can be addressed by a concentrated emphasis on evaluation of existing protocols for their adequacy for nanomaterial testing, followed by a focused medium-term effort to develop new test protocols as appropriate. Dose-response characterization work should begin in the near term, with ADME-related (adsorption, distribution, metabolism, and elimination) work beginning in the medium term. Work on mode of action should commence with a concerted effort toward the latter part of the near-term, and shift in the medium term to development of predictive tools including structure-activity relationships. This need will also be informed by the results of human health studies. Finally, tiered testing scheme development should commence with a heavy emphasis in the latter part of the near term as adequate test protocols become established.

A second high-priority set of research needs for the near term is associated with the second highest priority research need identified in the August 2007 Interim EHS Research Priorities document, namely, research related to principle sources of environmental exposures and exposure routes. For commercial nanomaterials in particular, this research will allow identification of appropriate biological and other environmental receptors that could be affected by the release of nanomaterials. Research on releases from nanomaterial manufacture and from nanomaterials that are incorporated into commercial products should have a near-term focus given the likelihood of significant releases

from these sources. Life cycle exposures subsequent to manufacture/product incorporation should begin in the latter part of the near-term period as more information becomes available to focus this research. Information from monitoring sources and exposures will be useful for distinguishing deliberate from unintentional releases. Retrofitting existing exposure models to accommodate nanomaterials, and developing new exposure models and estimation techniques is a high priority and will be emphasized as sufficient data become available. It is currently represented by very limited amounts of research.

Research on the two priority research needs for environmental transport and transformation is already represented by a substantial investment in fundamental research, and the two priority research needs are linked by common areas of investigation. For both of these areas, the emphasis on identification of key physical/chemical properties affecting transport and transformation should continue in the near term. A heavy emphasis on research on key transport and transformation processes should follow in the beginning of the medium term. Finally, work on models in these two areas must be ongoing as more information becomes available; an initial light emphasis should be placed on such predictive tools in the middle of the near-term, followed by a heavier emphasis in the medium term.

Although research on abiotic and ecosystem-wide effects was ranked as third highest priority in the initial ranking process, it has now moved to fifth priority. This is due to the overarching needs noted above (in particular the need to understand changes to nanomaterials as they contact environmental matrices). Further, an evaluation of abiotic and system-wide effects of nanoparticles may have to await additional fundamental research, including that from advances in research needs #1, #2, and #3. Studies on populations of key environmental receptors should begin with a heavy emphasis in the medium term as key receptors are identified by other ongoing research; higher-level community effects research should begin in the long-term time frame, and ecosystem/abiotic effects work should start in the latter portion of the long-term time frame.

Figure 7. Relative emphasis as a function of time for EHS priority research needs: Nanomaterials and the Environment category

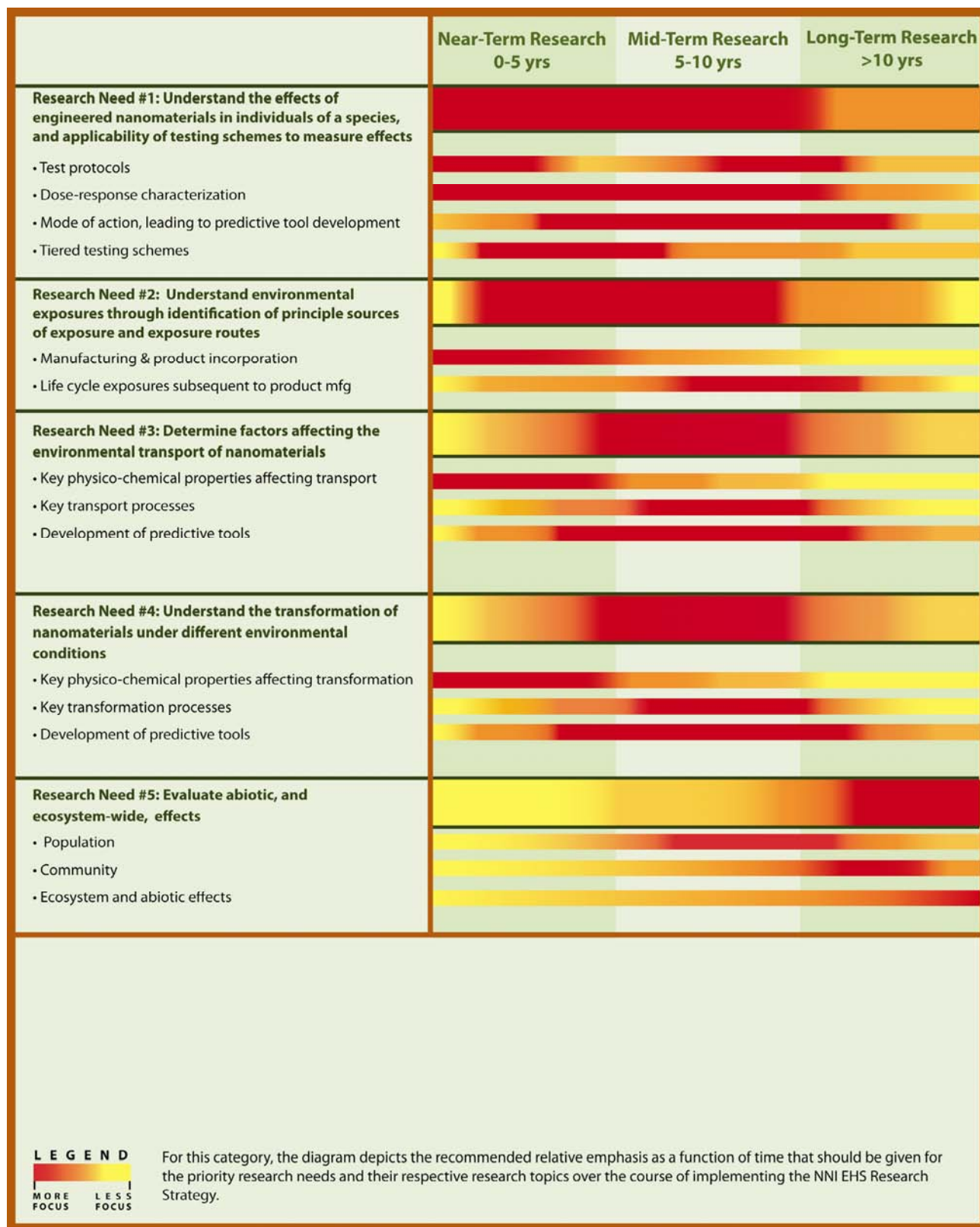
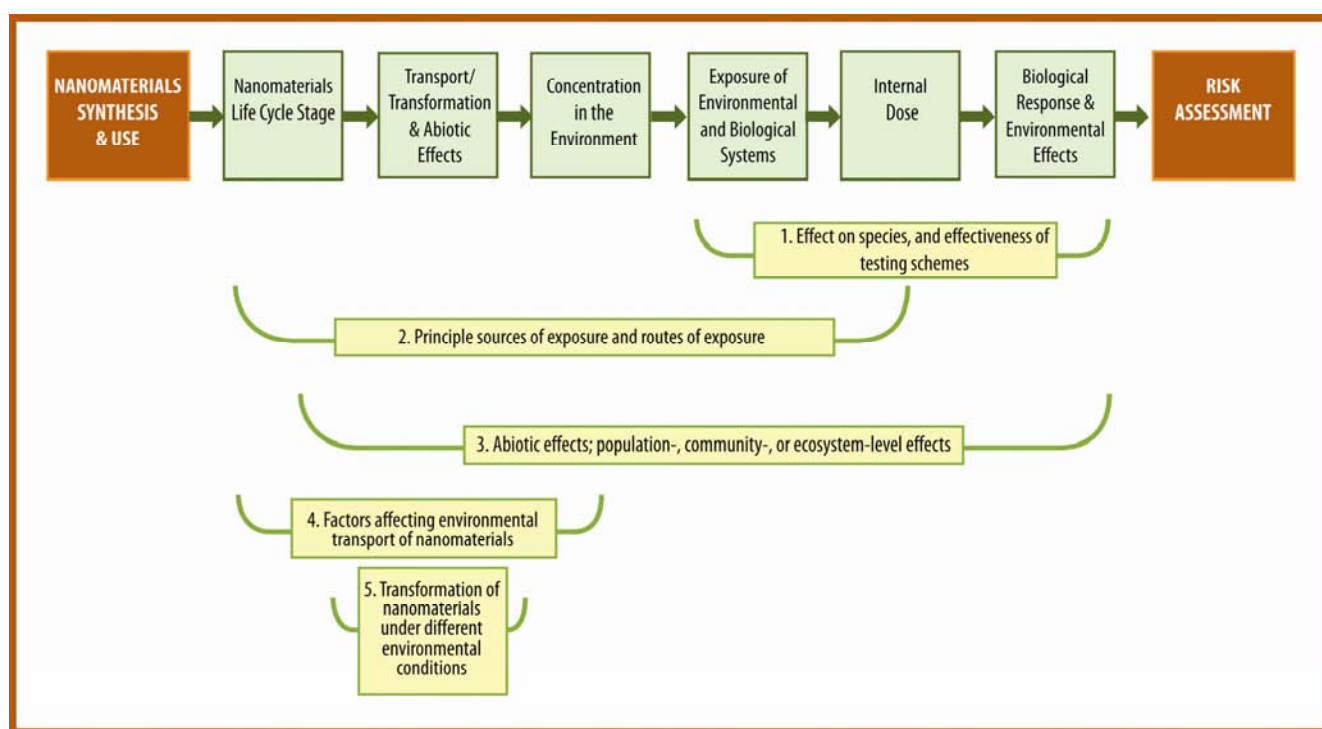


Figure 8 presents a conceptual framework for the relationship between Nanomaterials and the Environment research needs and the broader context of research supporting nanomaterials risk assessment. Nanomaterials and the Environment research has two different components related to potential adverse effects: (1) those that result in biological responses in individuals identified through testing a few relevant ecological receptors of a single species for their responses to a given nanomaterial, and (2) effects that could be manifested at the population, community, or ecosystem levels. These effects are only seen when exposures are sufficient to trigger such effects. Significant exposures can be better identified by examining the various life stages of a nanomaterial, from manufacture of the nanomaterial, to its incorporation into a commercial product, to use by consumers, to disposal. With releases at any point in the life cycle, potential adverse effects can be modified by transformation events, other interactions between nanomaterials and components of environmental matrices, and transport phenomena subsequent to release of the nanomaterial.

Figure 8. Framework for EHS research supporting Nanomaterials and the Environment*



* This diagram is not comprehensive and is only intended to qualitatively show the general relationships between the prioritized research needs within this category and phases of the simplified framework for research related to EHS and risk assessment of nanomaterials shown in Figure 2. The sizes of the boxes for the prioritized research needs are not intended to imply any differences in degree of emphasis or level of effort. The green lines extending outside the boxes indicate roughly the phases of the simplified framework that are to be addressed by each of the identified priority research needs of this category.

Research Category: Human and Environmental Exposure Assessment

Total estimated funding in FY 2006: \$1.1 million

Total projects: 5

Agencies supporting research in this category: DOD/AF, NIOSH, NSF

Prioritized EHS Research Needs for Human and Environmental Exposure Assessment	FY 06 funding Estimate \$K (% of total)	Number of Projects (% of total)
1. Characterize exposures among workers	879 (77%)	2 (40%)
2. Identify population groups and environments exposed to engineered nanoscale materials	--	--
3. Characterize exposure to the general population from industrial processes and industrial and consumer products containing nanomaterials	--	--
4. Characterize health of exposed populations and environments	--	--
5. Understand workplace processes and factors that determine exposure to nanomaterials	265 (23%)	3 (60%)
Multiple: Projects that capture multiple needs	--	--
Other: Not captured in needs above, but of benefit to the research category	--	--

Background

The priority research needs for this category identify work to enable the collection of exposure information. Data collection should group individuals into exposure categories and relate groups potentially exposed to nanomaterials, including workers, patients, consumers, and neighbors of production or utilization plants. Research should consider exposure assessment studies to quantify any general population exposures to nanomaterials resulting from the use of consumer products and to identify cases of unusual injury and patterns of health outcomes suspected of being associated with exposure to nanomaterials. Information on the process, task, and location variables should be evaluated to understand how nanomaterials behave in workplace environments and what factors determine the exposures to nanomaterials in such environments.

Summary of Analysis by Research Need**Research Need #1. Characterize exposures among workers**

The purpose of the first of two projects falling under this priority is to develop intramural surveys that will obtain fundamental data on workplace exposures related to nanotechnology. The second project aims at collecting exposure information for workers at facilities manufacturing and using nanoscale and microscale titanium dioxide particles. The study objectives are: (1) to develop a strategy to measure exposure to nanoscale particles and (2) to characterize exposure to nanoscale and microscale TiO₂ for various jobs and tasks at various facilities manufacturing and using TiO₂. The results of the study will be used by NIOSH in setting recommendations to protect workers exposed to nanoscale and microscale TiO₂.

Research Needs #2, #3, and #4

There were no projects identified under these priority research needs.

Research Need #5. Understand workplace processes and factors that determine exposure to nanomaterials

The three projects falling under this priority look at broad characterization and analysis of factors influencing exposures in the workplace and more specifically at the evolution of nanoparticles emitted by production equipment in the workplace environment and its effect on exposure potential.

The scope of one of the three projects under this priority is to foster the development of partnerships, exposure monitoring instrumentation, operational protocols, and a comprehensive and detailed database of nanoparticles and their properties. These activities are intended to provide the occupational safety and health community with a better understanding of the nature and extent of potential occupational exposures to nanoparticles. A second project will measure the fate of nanoparticles emitted through a leak in a nanoparticle production process into a workplace environment, focusing on changes of the nanoparticle surface area. The third project will identify factors that influence the generation, dispersion, and deposition of nanomaterials in the workplace. The risk of exposure via inhalation or dermal contact will be quantified for benchmark nanomaterials with well-defined physical and chemical characteristics.

Summary of Balance-Assessment for Human and Environmental Exposure Assessment Category

The task force identified the following common themes for this research category:

1. Priorities are intertwined within the same category and between categories
2. Collaborations between several agencies are critical to successfully address research priorities in this category
3. Continuous nature of surveillance research poses additional challenges in identifying time frames for research in this category

In FY 2006 the U.S. Government invested over \$1 million in research on Human and Environmental Exposure Assessment. Five projects cover two research needs, research need #1 (characterize exposures among workers) and research need #5 (understand workplace processes and factors that determine exposure to nanomaterials). These projects have relevance to other research categories such as Instrumentation, Metrology, and Analytical Methods, Nanomaterials and the Environment, and Risk Management Methods. In addition to research relevant to exposure assessment, a project funded by DOD/AF looks at evaluating personal protective equipment (PPE) and developing guidance on handling nanomaterials, which are covered by the Risk Management Methods category. On the other hand, there are projects listed in other research categories that have relevance to this category. Specifically, the project “Particle Surface Area as a Dose Metric,” placed in the Nanomaterials and Human Health research category, targets the identification of the proper metrics of exposure. There is also a project funded under the “NSEC: Network for Hierarchical Manufacturing” reported in the Instrumentation, Metrology, and Analytical Methods category that has critical relevance to exposure assessment and measurements.

The limited number of projects in this area mirrors to some degree the nascent nature of nanotechnology. Presently, only a limited number and volume of nanotechnology-enabled products are manufactured and marketed in the United States. Systematic collection of exposure information is hindered by the lack of standardized methods, reference materials, protocols, and field-ready and affordable instrumentation for exposure measurements. For example, health surveillance guidelines required to address research need #4 have become available in a draft form only recently and are only for occupational settings.⁵ As priority research needs are addressed in other categories, especially basic (e.g., the development of novel exposure measurement methods) and applied (e.g., translating unique measurements into routine field measurements) research in the Instrumentation, Metrology, and Analytical Methods

⁵ <http://www.cdc.gov/niosh/review/public/115/>

category, research in the Human and Environmental Exposure Assessment category can be conducted more effectively.

Greater efforts are needed to fully address all of the research priorities in this research category. In particular, emphasis should be placed on initiating research needed to address research needs #2, #3 and #4. In the near-term, research need #2, aimed at identifying population groups and environments exposed to engineered nanoscale materials, has the highest priority of these three research needs. This is because addressing this need will facilitate and optimize research in research needs #3 and #4 by identifying target population groups. Funding levels to address these research priorities are difficult to evaluate given the breadth of the scope of each priority and the large number of agencies that need to be involved with such work. Efforts under research needs #1 and #5 should be expanded to include exposure characterization and understanding of a wide range of nanomaterials in diverse workplace environments and processes through a complete product life cycle from nanomaterials manufacturing, to its incorporation into consumer products, to disposal and recycling.

**Figure 9. Relative emphasis as a function of time for EHS priority research needs:
Human and Environmental Exposure Assessment category**

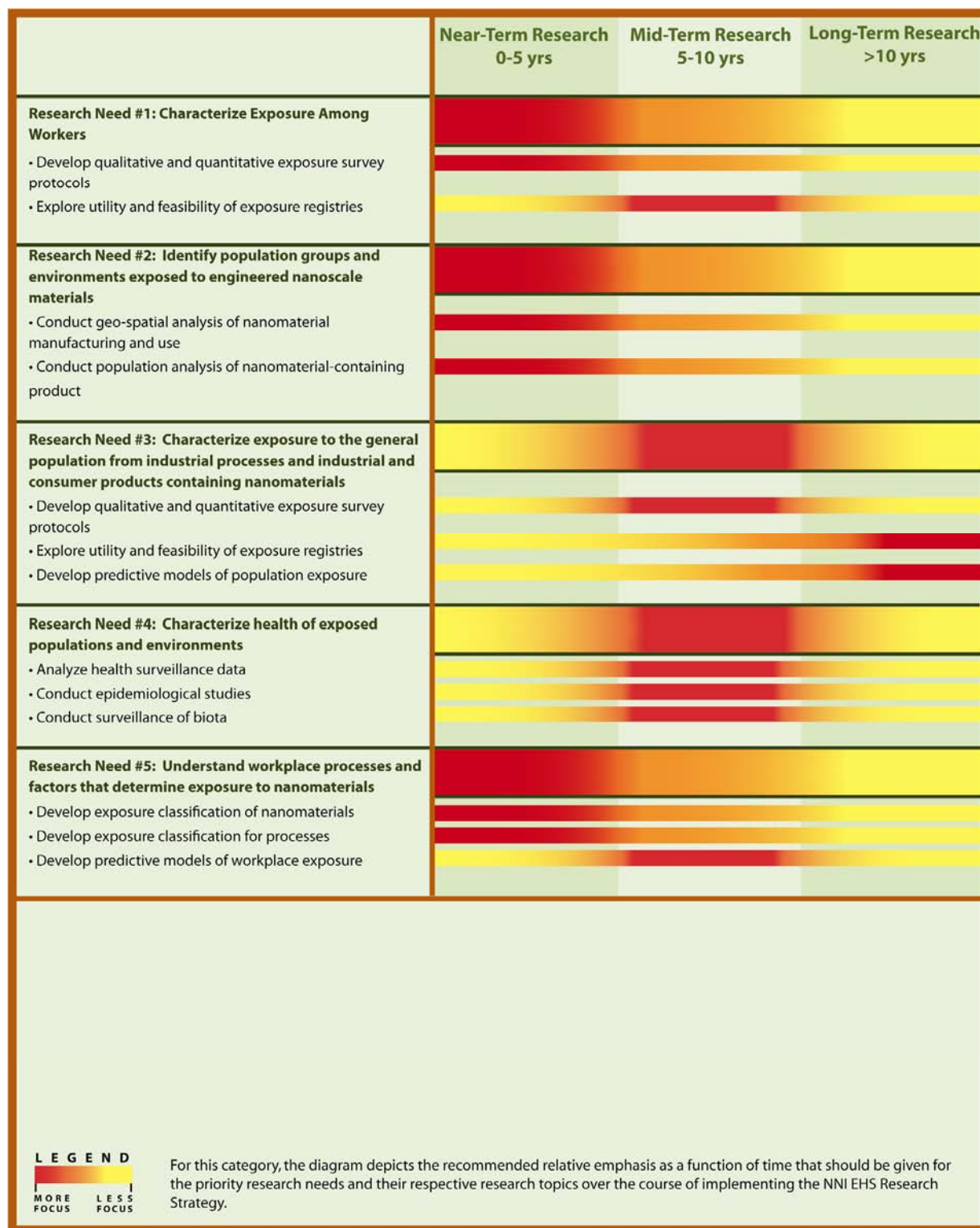
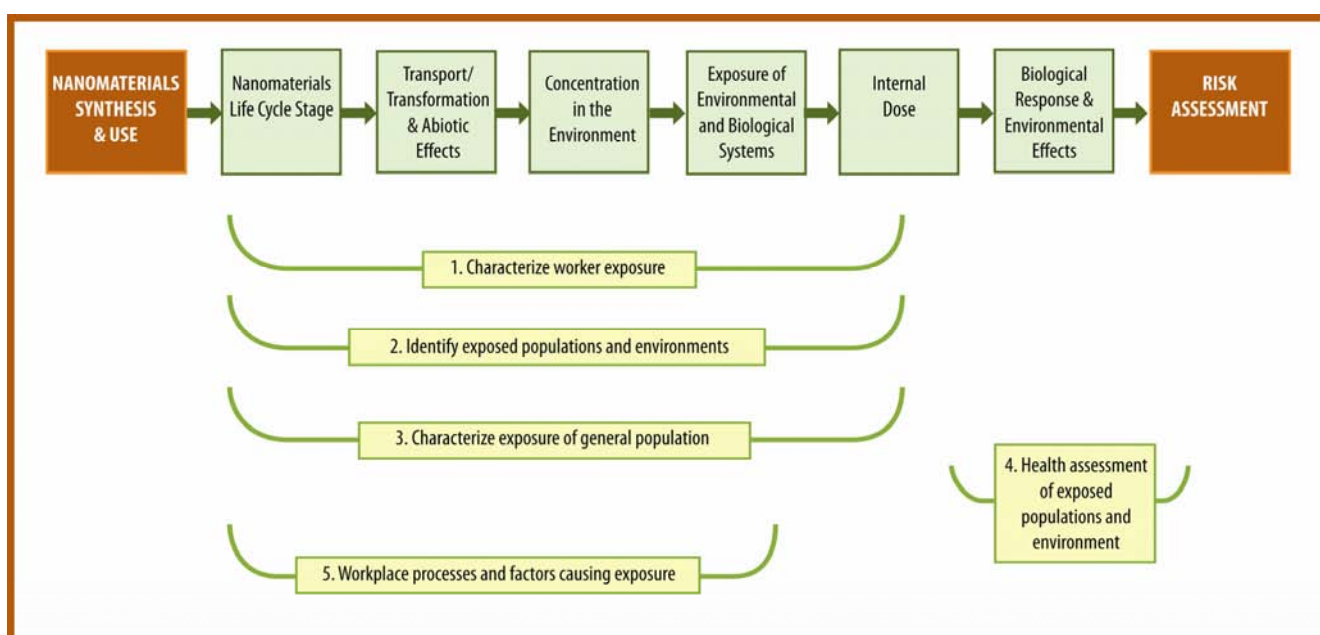


Figure 10 presents a conceptual framework for the relationship between Human and Environmental Exposure Assessment research needs and the broader context of research supporting nanomaterials risk assessment. Research in this category aims at characterizing exposures of workers, populations, and environments by measuring and modeling exposure levels and by monitoring biological response indicators. Exposures can be assessed at different points in the EHS research framework. Therefore, research needs in this category cross over all elements of the framework shown in Figure 10. Specifically research needs #1, #2 and #3 can be placed under the framework spanning from the Nanomaterials Life Cycle Stage element to the Internal Dose element, whereas research need #5 spans the framework from the Nanomaterials Life Cycle Stage element to the Exposure of Environmental and Biological Systems element. Research need #4 relates to the Biological Response and Environmental Effects element of the framework.

Figure 10. Framework for EHS research supporting Human and Environmental Exposure Assessment*



* This diagram is not comprehensive and is only intended to qualitatively show the general relationships between the prioritized research needs within this category and phases of the simplified framework for research related to EHS and risk assessment of nanomaterials shown in Figure 2. The sizes of the boxes for the prioritized research needs are not intended to imply any differences in degree of emphasis or level of effort. The green lines extending outside the boxes indicate roughly the phases of the simplified framework that are to be addressed by each of the identified priority research needs of this category.

Research Category: Risk Management Methods

Total estimated funding in FY 2006: \$3.3 million

Total projects: 14

Agencies supporting research in this category: DOD/AF, EPA, NIOSH, NSF

Prioritized EHS Research Needs for Risk Management Methods	FY 06 funding Estimate \$K (% of total)	Number of Projects (% of total)
Overarching Research Priority: Evaluate risk management approaches for identifying and addressing risks from nanomaterials		
1. Understand and develop best workplace practices, processes, and environmental exposure controls	495 (15%)	4 (29%)
2. Examine product or material life cycle to inform risk reduction decisions	396 (12%)	2 (14%)
3. Develop risk characterization information to determine and classify nanomaterials based on physical or chemical properties	132 (4%)*	1 (7%)*
4. Develop nanomaterial-use and safety-incident trend information to help focus risk management efforts		
5. Develop specific two-way risk communication approaches and materials	231 (7%)	1 (7%)
Multiple: Projects that capture multiple needs	2,046 (62%)	6 (43%)
Other: Not captured in needs above, but of benefit to the research category		

**This project addressed needs 3 and 4 roughly equally*

Background

All the research projects identified under this category address the overarching research need to evaluate risk management approaches for identifying and addressing risks from nanomaterials. Research in this category focuses on methods for risk management of nanomaterials, including but not limited to, research on methods to reduce exposures to potentially hazardous nanomaterials; research to improve procedures for risk and accident avoidance; research to improve work practices, engineering controls, and protective equipment; and research to develop procedures for life cycle assessment.

Rather than being separable to one or more of the five specific research priorities, approximately two-thirds of the funding and nearly half of the projects of this category are directed at the overarching need expressed in the Interim Research Priorities document. The focus of much of the funding at such a general level may be appropriate for some sectors of nanotechnology EHS risk management research, given the elementary stage of current understanding of the need for new risk management approaches. For example, it may first be necessary to step back and ask general questions regarding whether current risk management approaches are relevant and then parse out individual issues on the basis of that analysis.

Most of the projects identified as relevant to the Risk Management Methods (RMM) category were funded by NIOSH or NSF, which might be interpreted as a need for additional funding by agencies that undertake risk management. However, the apparent lack of funding by regulatory agencies for risk management methods research could be due to the data call having been focused primarily at grant-related efforts for a topic that may not always be addressed through research. The effectiveness of risk management approaches is likely to be addressed in many cases through agency analysis rather than through funded research. For example, several agencies have expended resources

in the evaluation of risk management methods through workshops, task force efforts, white papers, peer reviews, and public meetings. While these more applied methods of evaluation would not be entirely captured as research, they should nonetheless be considered as part of the research need category as expressed in the September 2006 EHS Research Needs document.

Therefore, when considering gaps for these needs it should be noted that relevant sources of information will be developed through government funding that may not be captured through the annual OMB data calls for NNI funding by program component area or through evaluation of grant funding. Basic and detailed data collection under EPA's stewardship program will yield information relevant to this research need as well. Furthermore, data collection efforts through product development and review through FDA, EPA (e.g., pesticides), and other regulatory efforts are likely to generate information relevant to RMM priority research needs. The evaluation of gaps for RMM needs should collect such information and consider its relevance to the specific research needs.

It is difficult to correlate the need for additional resources with the identified research needs. For example, conceptual analysis of existing risk management methods is not necessarily a research-intensive item. Research needs #1, #2, and #3 are of a distributed nature (for example, workplace controls and life cycle analyses are likely to be specific to a large number of independent contexts and so would need to be developed independently), and so would seem to require more resources than research needs #4 and #5. Research need #3, developing hazard characterization information necessary for hazard management (for example in transport labeling or spill containment planning) would be substance-specific and also involve baseline research into material properties and hence would require either substantial resources or input from the other research categories.

Summary of Analysis by Research Need

Research Need #1: Understand and develop best workplace practices, processes, and environmental exposure controls

There are four projects falling under this priority research need. They are general in nature with respect to nanomaterials; however, the primary focus is on airborne particles and controls directed at inhalation exposures.

The functionality of specific risk control methods, such as a respirator and personal protection equipment, is being considered in the projects that have direct relevance to exposure mitigation. Particulate materials can to some extent be addressed in a general way for respiration, so research and development into these control measures should have wide application to many nanomaterials. As such, the work in this priority research need has a relatively high likelihood of utility and broad application. One project is also examining specific characteristics of ultrafine (nanoscale) metallic particles generated in automobile manufacture. This attention to particle characteristics in specific risk management considerations is important. Broad evaluation of practices and needs is also being addressed, which is a necessary prerequisite to identification of priorities for additional and more specific evaluations of scenarios and approaches to risk management.

Since this priority is focused on workplace safety, it is understandable that NIOSH is the only funding agency for occupational safety and health research. While the topics being funded are appropriate, ranging from specific evaluation of respirator function to broad evaluation of practices and needs, it appears that the funding is just beginning to address the potentially wide range of scenarios and methods that could be evaluated with respect to specific novel needs for risk management methods in the workplace. For example, dermal and ingestion exposure routes were not included in FY 2006 funding and should be considered. Segregation of analysis to types of particles and to classes of mitigation methods aimed at types of particles has been initiated for automobile manufacture, but should be extended to other particle types and scenarios, based, for example, on expected hazard or persistence. Because the number of scenarios is large, a necessary prerequisite to this expansion of evaluation would be consideration of the priorities across potential scenarios.

Research Need #2: Examine product or material life cycle to inform risk reduction decisions

There are two projects identified under this EHS priority research need, funded by EPA and NSF. These projects appropriately consider both the general case and specific cases of life cycle analysis (LCA). The EPA-funded project is more general in nature but directed at manufacturing technologies rather than particular product types, and the NSF project is directed at a sector of products (photovoltaics).

Gaps may exist in the particular application of LCA evaluation to product classes that are not covered by the two approaches and projects. A systematic evaluation (such as may occur through the projects funded under the overarching research priority) is needed to evaluate where the most critical of such gaps would exist.

Research Need #3: Develop risk characterization information to determine and classify nanomaterials based on physical or chemical properties, and

Research Need #4: Develop nanomaterial-use and safety-incident trend information to help focus risk management efforts

Research needs #3 and #4 are addressed roughly equally by one project. The NIOSH “Nanoparticle Information Library” (NIL) project seeks to collect, on a voluntarily submitted basis, data on nanomaterial characterization and uses. It will generate some information relevant to risk-based classification of nanomaterials (research need #3) and to use-trend information (research need #4).

Research needs #3 and #4 are not fully addressed by the research funded in FY 2006, representing a gap in the research. No projects related to identifying safety incidents were identified in the funding. Because the data in the NIL project is based on voluntary submissions, it is unlikely to provide comprehensive or consistent coverage of either risk characterization information or trend information on uses. More comprehensive and consistent data across types of materials and industrial sectors is needed so that the information can be used to inform risk management needs.

Research Need #5: Develop specific two-way risk communication approaches and materials

The one project identified under this priority research need will develop communication products such as websites, NIOSH numbered documents, technical publications, and presentations, to communicate and disseminate research results and recommendations on health and safety issues involved in nanotechnology. It will also foster development of key stakeholder partnerships in the manufacturing sector to effectively disseminate the products of the project.

This research need was only being addressed by one agency in the FY 2006 funding, and that project addresses only workplace-related issues. Furthermore, the project addresses specific dissemination of risk-communication-related materials, rather than the evaluation of risk communication issues and approaches that may be specific to nanotechnology applications. More widespread attention to the need should be initiated, at least in the sense of evaluating whether and what risk communication methods or materials specific to nanomaterials may be warranted. However, the general evaluations of risk management methods being carried out by the bulk of the funding under this category is likely to address some of this baseline evaluation of what is needed.

Projects Classified as Addressing Multiple Research Needs

Many of the projects under the Risk Management Methods category address the overarching research need, “Evaluate risk management approaches for identifying and addressing risks from nanomaterials” rather than under specific priorities. The 6 projects have broad scopes with regard to evaluation of factors that feed into risk management and so may provide additional information and perspectives to those of the general considerations of the NNI EHS Research Needs document. This additional information may provide independent viewpoints that will potentially provide greater assurance of complete consideration of what is important and relevant to identifying and managing risks. The broad evaluation of risk management approaches and needs is also a prerequisite to

prioritized selection of more detailed analysis of specific scenarios under which risk management methods may need evaluation and attention.

The projects seek to provide information and promote collaborations on general questions ranging from ethics and public perception, to frameworks for addressing risk evaluation and management, to evaluation of regulatory and legislative frameworks, and consideration of net benefits of the development of the technology. An important consideration for this level of funding and the general nature of the tasks may be whether the projects will overlap and be inefficient or seem contradictory. It is also difficult to ascertain what portions of the funding are directly relevant to the RMM research category, though all projects seemed to have components with high relevance.

It should be noted that issues not typically thought of as pertaining directly to risk management needs, such as ethics and societal considerations, are included in the projects that fall under this category. The relevance of these topics to research priorities is neither clarified nor dismissed in the present analysis and should be the subject of further evaluation.

Summary of Balance-Assessment for Risk Management Methods Category

The balance of funding in FY 2006 for Risk Management Methods research is weighted toward general analyses of approaches rather than toward specific activities. Furthermore, the specific activities that are represented, such as evaluation of respirator materials in workplace settings, tend to focus on occupational controls and inhalation exposures within the occupational setting. While the focus on occupational inhalation exposures is fitting, given that worker populations are likely to be the first affected in product development and production, future funding should also include other scenarios and other exposure pathways. The selection of those scenarios and the pathways to be included should follow from activities such as life cycle analysis over a broader range of materials than was seen in the FY 2006 funding. They should also follow from general evaluations of the existing risk management approaches, so that scenarios and pathways are chosen that represent the greatest use of resources to reduce potential risks.

Trend information, and even current information, on uses of nanoscale materials in commerce and consumer products is generally not addressed in FY 2006 funding, and is lacking. Trend and use information is of critical importance to comprehending current and future exposure potential and scenarios in which risk management methods or practice changes may be needed. On balance, future year funding should be increased for developing trend and use information.

Stemming somewhat from this lack of use and trend information is a similar lack of risk characterization information that could feed into risk management methods. Risk management methods that could use this kind of information, for example, include exposure controls or even simpler methods and needs such as Material Safety Data Sheets with regard to changes in exposure limits. Another example is Department of Transportation hazardous material placards in cases where flammability or reactivity is affected by particle size. The development of this kind of information should receive a higher emphasis in future year funding.

Figure 11 presents relative emphasis as a function of time for the prioritized research needs. The sub-bars under each of the 5 main research needs represent relative timing information for details of research needs that were included in the September 2006 NNI EHS Research Needs Document.

**Figure 11. Relative emphasis as a function of time for EHS priority research needs:
Risk Management Methods category**

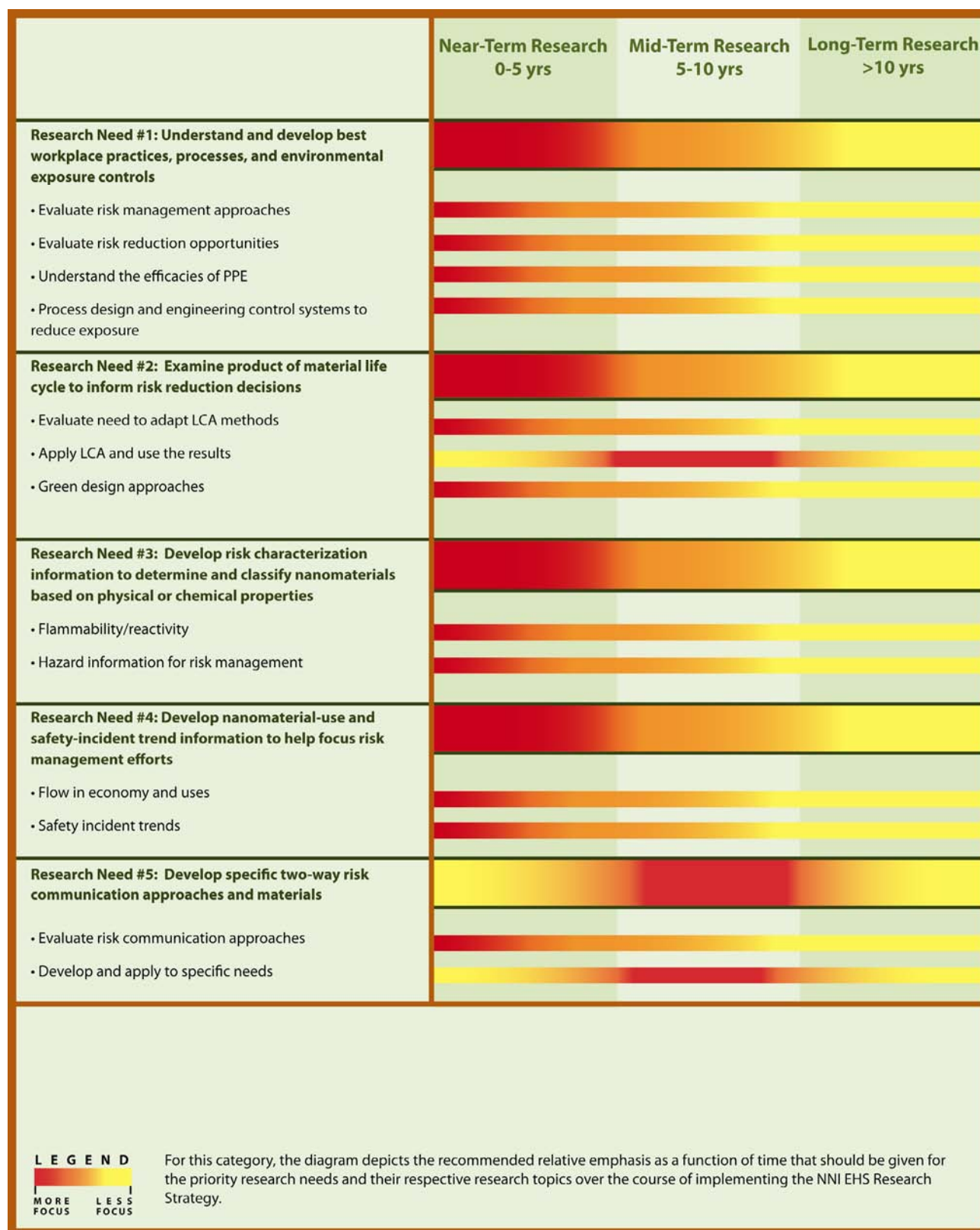
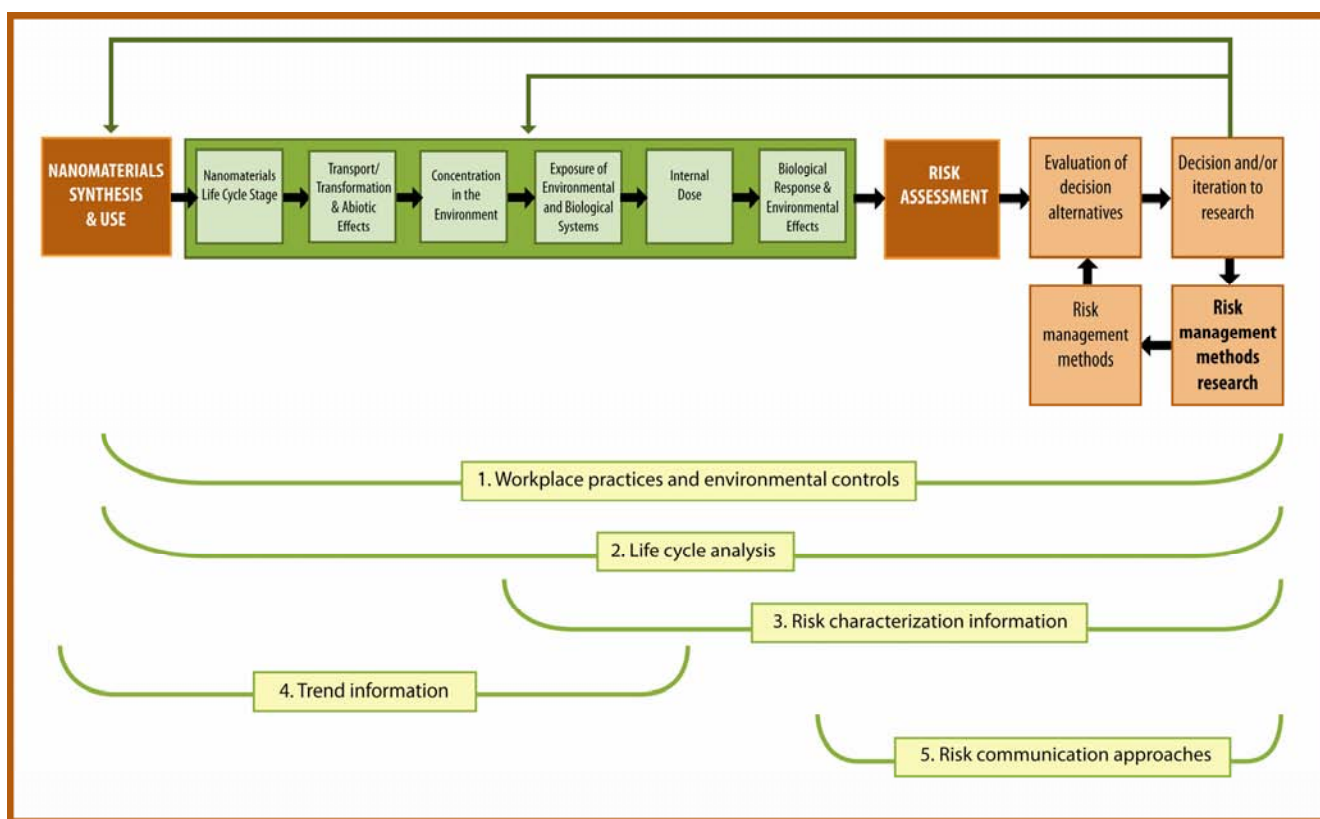


Figure 12 presents a conceptual framework for the relationship between Risk Management Methods research needs and the broader context of research supporting nanomaterials risk assessment. Any research to support decisions is at least in principle preceded by a decision need, which then, to the degree necessary would stimulate either the collection of existing data (literature review) or the development of new data that would be applied to a risk assessment. The risk assessment scope would be shaped both by the decision need and to some degree by the available data. The risk assessment would then be considered along with risk management methods to lead to a decision among risk management alternatives. The ability to make a decision may be affected by the level of certainty of the conclusions with regard to the outcomes of the alternatives. Research could be called for at the decision phase instead of, or in addition to, selection of a risk management alternative. The numbered boxes in Figure 12 refer to the priority research needs identified in this document for the Risk Management Methods category.

Figure 12. Framework for EHS research supporting Risk Management Methods*



* This diagram is not comprehensive and is only intended to qualitatively show the general relationships between the prioritized research needs within this category and phases of the simplified framework for research related to EHS and risk assessment of nanomaterials shown in Figure 2. The sizes of the boxes for the prioritized research needs are not intended to imply any differences in degree of emphasis or level of effort. The green lines extending outside the boxes indicate roughly the phases of the simplified framework that are to be addressed by each of the identified priority research needs of this category.

Current Balance of Nanotechnology-Related EHS Research Investment

In the years FY 2005 through FY 2007, the NNI invested over \$120 million in EHS research as defined and reported in the annual NNI budget supplement documents. The NNI agencies estimate spending \$58.6 million on EHS research in FY 2008 and have requested \$76.4 million in the President's Budget for FY 2009. As noted previously, the annually reported EHS research figures do not capture all of the research that is related to the research needs discussed in this document. This is due to the fact that EHS research spending reported in the budget supplement is for research that is primarily focused on understanding potential risks. It does not include research that is aimed primarily at applications or at characterization and measurement of nanomaterials, much of which also has utility for EHS risk assessment and risk management. The amount estimated for FY 2006 EHS "primary purpose" research in the annual NNI Supplement to the President's FY 2007 Budget was \$37.5 million.⁶ However, the total amount spent on research related to the EHS priority research needs in FY 2006 as reported in preceding sections of this document is \$68 million—nearly 80 percent more than the "primary purpose" figure. A large fraction of the additional research effort is that reported under the category of Instrumentation, Metrology, and Analytical Methods and, to a lesser extent, under the category on Nanomaterials and Human Health. The data for EHS spending in FY 2006 show a wide variation in funding levels and the numbers of projects among the five research categories. Although the five broad categories of priority EHS research (Table 1) have not been prioritized with respect to each other, there is consensus that the Instrumentation, Metrology, and Analytical Methods category is cross-cutting, supporting research in every other category, and therefore are generally a high priority. Likewise, there are high-priority areas of research on Nanomaterials and Human Health and on Nanomaterials and the Environment, as described in Section II. Research on Human and Environmental Exposure Assessment and on Risk Management Methods is recognized as critical to risk assessment and risk management. However, some of the research in these areas requires input from other research categories. Therefore, it is appropriate that investments at this time are predominantly in the categories of Instrumentation, Metrology, and Analytical Methods, Nanomaterials and Human Health, and Nanomaterials and the Environment. The balance of spending will evolve in time as research programs mature and efforts that are undertaken sequentially are initiated.

The current and future research that is within the scope of the five EHS research categories is diverse in a number of dimensions. This research is highly multidisciplinary, involving researchers from many fields such as chemistry, materials science, biology, engineering, computer science, and medicine. It ranges from basic research to increase fundamental understanding of the properties and behavior of nanomaterials in various environments to applied research, such as development of instrumentation for cost-effective measurement of workplace exposure to nanomaterials. There is research that should continue to be supported in the near term and research that need not or cannot be initiated until a future date when additional capabilities or information is available. Finally, the breadth of research that is covered by the 2006 EHS Research Needs document calls for a similarly broad range of activities by many entities—various agencies, industry, and other governments.

⁶ http://www.nano.gov/NNI_07Budget.pdf

III. Framework for Addressing EHS Research Needs

Introduction

Addressing the priority research needs that are identified in this report will continue to require the coordination, cooperation, and commitment of the multiple agencies that support research and/or use the resulting information. This document has been developed with the participation of all these agencies and represents an overarching assessment of the near-term and long-term EHS research needs as presently understood that will support risk assessment and risk management of nanomaterials.

It is essential in this process to maintain perspective on the overarching opportunities in nanotechnology-related EHS research that cut across the five categories and the needs delineated under each of those categories. Continuing basic research to understand fundamental biological responses to nanomaterials remains one such overarching opportunity. For example, modeling and simulation development based on first principles (i.e., more analytical than empirical) will significantly advance nanotechnology-related EHS research. Similarly, establishing consensus-based standards, such as minimum data sets for particular nanomaterials and classes, will broadly facilitate integrative and progressive EHS research. Seizing these broad opportunities in parallel with addressing particular research needs will collectively shorten nanomaterial development timelines and streamline decision making on toxicity and other EHS implications. These opportunities constitute priorities in parallel with identified research gaps and highlight the need to maintain a broad-based, balanced investment.

Summary and Prioritization of Selected Research Needs

Based on this analysis of the FY 2006 snapshot of Federal funding for nanotechnology-related EHS research, needs for new or increased research efforts have been identified in several areas. To address these gaps, rebalancing within and among these five research categories, particularly in the near term, should focus on the following:

Instrumentation, Metrology, and Analytical Methods (all near-term)

- Develop analytical methods for identifying and measuring the critical parameters related to nanomaterials in biological systems, the environment, and the workplace
- Develop new quantitative nanoscale metrologies and databases of properties
- Develop methods for standardizing assessment of particle size, size distribution, shape, structure, and surface area
- Increase efforts to develop certified reference materials, specifically for toxicology and environmental studies

Nanomaterials and Human Health

- Develop and validate methods to quantify dose-response or structure-activity relationships, including parameters (near-term; links strongly to metrology)
 - Determine measurement parameters relevant for classes of nanomaterials (in priority order based on reasonable expectation of exposure)
 - Develop methods to quantify and characterize biological response
- Translate *in vitro* test results into *in vivo* models
- Extrapolate data to human exposures (mid- to long-term)

Nanomaterials and the Environment

- Evaluate and modify currently accepted test protocols for assessing effects in individual biological receptors, and improve dose-response characterization

III. Framework for Addressing EHS Research Needs

- Identify principle sources of, and routes for, exposure to environmental receptors based on nanomaterial/commercial product manufacture
- Identify key physical/chemical properties affecting transport/transformation of nanoparticles

Results from these near-term efforts should assist in later development of new test protocols for assessing effects in biological receptors; improve understandings of ADME (absorption, distribution, metabolism, and excretion) in relevant receptors; and development of predictive tools and robust testing schemes to streamline reviews of commercial nanomaterials. In the areas of exposure, and transport and transformation, again predictive tools and models should result which increases the ability to judge the overall exposures to commercial nanomaterials throughout their life cycles. Finally, work from all of these areas will contribute to evaluating the potential for higher-level environmental effects.

Human and Environmental Exposure Assessment

- Identify population groups and environments exposed to engineered nanoscale materials
- Characterize exposure to the general population from industrial processes and industrial and consumer products containing nanomaterials
- Characterize health of exposed populations and environments

Risk Management Methods

- Develop risk characterization information to determine and classify nanomaterials based on physical or chemical properties
- Develop nanomaterial-use and safety-incident trend information to help focus risk management efforts
- Expand exposure-route-specific risk management methods research and life cycle analysis research on the basis of nanomaterial use scenarios expected to present greatest exposure and potential for health or environmental effects

Particular emphasis should be given to the development of methods to detect nanomaterials in biological matrices, the environment, and the workplace. The need for this research emphasis spans the entire framework, from the synthesis and use of nanomaterials to the detection and characterization of materials as a function of exposure.

The member agencies have examined each of these particular needs carefully, and with respect to each gap, the agencies have agreed within the interagency context to assume the roles identified below to address these gaps in a manner consistent with their specific missions and available resources.

Implementation of Strategy for Nanotechnology-Related EHS Research

The framework for implementation outlined below describes the various activities and coordination needed to address these gaps as well as the full spectrum of NNI EHS research. It also provides for participation, interaction, and partnership with non-Federal stakeholders to leverage efforts and to expedite progress.

- **Support broad base of research to facilitate regulatory decision making and to expand the horizons of nanotechnology-based applications for health and the environment.** The EHS research strategy fundamentally depends on sustaining the broad spectrum of basic research, with support from agencies that fund basic research on the fundamental properties of nanomaterials (including NSF, DOE, NIST, and NIH). The current balance of research funding addresses such basic investigations and supports regulatory decision making. Gaps identified in the research that supports regulatory decision making should not be addressed at the cost of broad-based fundamental research—to do so would ultimately undercut the U.S. nanotechnology initiative as a whole.
- **Coordinate existing, and foster expanded, agency efforts to address priority EHS research needs and identified gaps.** The NEHI Working Group will continue to facilitate coordination and increased collaboration among the

III. Framework for Addressing EHS Research Needs

NNI agencies' research programs to address priority research needs both individually and jointly, leverage investment and expertise, and avoid duplication of effort within each research category.

- Convene workshops addressing each research category over the timeframe 2008-2010 to assess the state of science, current research, and to reassess areas of weakness and gaps. Participants will include, for example, representatives from both contributor and user NNI agencies, academia, non-governmental organizations, and industry
- Facilitate development of joint programs among NNI member agencies to address research needs of mutual interest
- Clarify priorities and areas of focus for pursuit and collaborations
- Avoid unproductive redundancy and research that is decoupled from real-world application
- Identify synergistic opportunities
- **Establish regular review process.** The NEHI Working Group will conduct periodic progress review and will update the research needs and priorities, taking into consideration advances from private sector and international entities.
- **Facilitate partnerships with industry.** The NEHI Working Group will explore and develop mechanisms with participating agencies for partnering with industry to support priority research that reduces risk uncertainty facing the range of businesses and industry sectors that are commercializing nanomaterials for beneficial and practical applications. One example is the proposed NIH NanoHealth Enterprise, an interdisciplinary cross-sector program to integrate critical materials science and biology research and support informatics and training needs for the safe development of nanoscale materials and devices. Organizations like the Foundation for the NIH may provide appropriate authority and structure to facilitate and execute such partnerships.
- **Coordinate efforts internationally.** Participate actively in international efforts related to EHS research, particularly in the work of the OECD Working Party on Manufactured Nanomaterials (WPMN), e.g., WPMN efforts to develop internationally agreed EHS research priorities, testing protocols, and predictive tools.
- **Focus on development of consensus-based documentary standards to support oversight of nanomaterials research.** Participate in and support efforts by national and international standards development organizations to develop nanotechnology-related documentary standards, particularly those related to EHS research.
- **Facilitate wide dissemination of research results.** Participate in and support activities aimed at broadly disseminating available information about EHS aspects of nanomaterials. Such activities include those already underway in the OECD WPMN, and the ISO Technical Committee on Nanotechnologies (TC 229) Working Group on Health, Safety, and Environment.

Interagency Coordination to Address Nanotechnology-Related EHS Research Needs

In addition to the investments by individual agencies, Federal spending on nanotechnology-related EHS research also includes coordinated interagency research activities and solicitations. This interagency document will guide programs and investment decisions in the coming years, including investments by the individual agencies and coordination of interagency activities. In fact, the priorities identified in the 2006 EHS Research Needs document and participation of program managers in the development of that document already have influenced agency planning. However, because the agencies have varied missions, their individual priorities may differ in scope and focus from those outlined in this report. Annual spending by each agency for nanomaterials EHS research will be guided by not only the priorities described in this document, but also by agency-specific missions, priorities, and needs. For this reason, strong interagency coordination is essential.

The NEHI Working Group is perhaps unique among interagency bodies focused on research in taking the needs of regulatory agencies into account in setting priorities for research. Moreover, the regulatory agencies can benefit as users of the research results and as participants in the ongoing efforts to coordinate and prioritize the broad interagency research programs.

As stated in the 2007 NNI Strategic Plan, “The NNI consists of the individual and cooperative nanotechnology-related activities of twenty-five Federal agencies with a range of research and regulatory roles and responsibilities. ... The NNI as a program does not fund research; however, it informs and influences the Federal budget and planning processes through its member agencies.”⁷ In the context of this document, both statements hold true for nanotechnology-related EHS research as one component of the overall research and development portfolio coordinated through the NNI.

With this understanding and within the roles and responsibilities stated in the charters for the NSET Subcommittee and the NEHI Working Group, member agencies of the committee and working group have agreed among themselves to assume the roles indicated in Table 2 to move the Federal efforts in nanotechnology-related EHS research forward. There are three roles identified for the agencies for each of the five categories: (1) coordinating agencies, indicated by a ♦ in the table, are those agencies that have agreed to take a leadership role in coordinating and communicating with other NNI member agencies concerning agency needs and the ongoing adaptation of NNI research priorities to new discoveries and new materials; (2) contributing agencies, indicated by a ● in the table, are those that have funded or are planning to fund or conduct research within their missions that is expected to contribute knowledge, information, or new discoveries to the category; and (3) user agencies, indicated by a ■ in the table, are those that have expressed a need for, or expectation to make use of, research outputs or information to support their agency’s missions and responsibilities, whether those be mission agency research needs or regulatory agency needs for information to support their regulatory decision making.

⁷ http://www.nano.gov/NNI_Strategic_Plan_2007.pdf

Table 2. Roles of NEHI Working Group Member Agencies with Regard to Nanotechnology-Related EHS Research Needs

◆ – Coordinating Agency ○ – Contributor □ – User

All coordinating agencies have roles as contributors to and users of the research from the respective categories, with the exception of FDA, which has the roles of coordinating agency and user.

	Research Need	Instrumentation, Metrology, and Analytical Methods	Nanomaterials and Human Health	Nanomaterials and the Environment	Human & Environmental Exposure Assessment	Risk Management Methods
Agency						
NIH		○□	◆	□	□	
NIST		◆	○	○	○	○
EPA		○□	○□	◆	○□	◆
FDA		□	□	□	□	◆
NIOSH		○□	○□	○	◆	○□
NSF		○*	○*	○*	○*	○*
DOD		□	□	○□	□	○□
DOE		○□	□	○□	□	□
USDA		□	○□	○□	□	□
DOT			□	□	□	□
OSHA		□	□		□	□
CPSC		○□	□	□	○□	○□
USGS		○□		○□	○□	

*NSF is a contributor according to the mission of the agency covering the upstream, fundamental research on utilization, implications, and risk mitigation of nanotechnology, infrastructure, and education.

The NEHI Working Group represents a strong network of individuals across the Federal Government. In many instances, agency representatives to the NEHI Working Group are representing intra-agency networks, such as the FDA Nanotechnology Task Force. In the Office of Management and Budget, one person is identified as responsible for coordinating with the budget examiners for all of the NNI agencies to assess EHS and other research government-wide. This highly interconnected “network of networks” is both flexible and robust in its capacity to support the NNI EHS research program. The functional aspects of this network are supported by the staff members of the National Nanotechnology Coordination Office (NNCO).

The NEHI Working Group network provides a forum for exchanging information among participants concerning agency-specific research programs and the broad range of activities related to nanomaterials. It also has led to two joint interagency EHS research solicitations.

The overall NNI EHS research strategy also directly relies on the activities and plans of individual agencies with respect to their respective missions and areas of focus. Table 3 below briefly summarizes many of these activities and highlights.

Table 3. Nanotechnology-Related EHS Research Activities and Highlights, FY 2008

Agency	Nano EHS Research, Activities, Plans, and Strategic Efforts (individual and joint)
EPA	<ul style="list-style-type: none"> ▪ <i>Nanoscale Materials Stewardship Program</i> launched, January 2008. ▪ <i>Nanomaterial Research Strategy</i> (in development). ▪ Joint solicitation led by NIH/NIEHS, with EPA and NIOSH as partners, focused on biocompatibility and including participation by five other NIH institutes. ▪ Collaboration with NSF and DOE will result in the awarding of an additional \$4 million to support health impacts research in the first half of 2008 to support research on fate/transport/transformation of nanomaterials and on human exposure/bioavailability of nanomaterials. ▪ Research funded: over \$31 million (as of FY 2007) of relevant research since NNI inception (\$12.2 million supporting projects on environmental applications of nanotechnology and \$19.8 million supporting projects to study potential health and ecological impacts). ▪ Through a recently initiated in-house nanotechnology research program, EPA scientists are developing increased collaborations with researchers at other Federal agencies, academia, and industry in order to broaden both the scope and results of EHS research. ▪ Development of EPA Nanotechnology White Paper, http://www.epa.gov/OSA/nanotech.htm. ▪ http://www.epa.gov/oppt/nano/ and http://es.epa.gov/ncer/nano/.
FDA	<ul style="list-style-type: none"> ▪ Continue to develop responses to the 2007 FDA Nanotechnology Task Force report. ▪ Continue collaboration with the National Cancer Institute's Nanotechnology Characterization Laboratory. ▪ Seek to develop collaborative research relationships through exploration of public/private partnerships. ▪ Continue efforts aimed toward international harmonization and collaboration of, for example, research efforts, testing protocols, and standardization of terminology and nomenclature, through available bilateral cooperation mechanisms and as necessary through multilateral organizations such as the Organization for Economic Cooperation and Development (OECD), CODEX ALIMENTARIUS, the International Council on Harmonization, and other similar organizations. ▪ Continue participation in nanoscale material toxicity research funded through the National Toxicology Program. ▪ http://www.fda.gov/nanotechnology/.
NIOSH	<ul style="list-style-type: none"> ▪ Research to obtain data relevant for drafting interim guidance on medical screening of workers potentially exposed to manufactured nanomaterials. ▪ Nanotechnology Field Teams site visit partnering industrial, academic, military, and research organizations to conduct baseline assessments of occupational exposure to engineered nanomaterials (17 to date).

III. Framework for Addressing EHS Research Needs

Agency	Nano EHS Research, Activities, Plans, and Strategic Efforts (individual and joint)
	<ul style="list-style-type: none"> ▪ Updating <i>Strategic Plan for NIOSH Nanotechnology Research</i>, originally released in 2005, by assessing the state of knowledge in occupational safety and health aspects of nanotechnology and conducting a critical gap analysis of research needs using <i>Progress Toward Safe Nanotechnology in the Workplace</i> (http://www.cdc.gov/niosh/docs/2007-123/). The updated strategic plan will outline NIOSH strategy to lead the occupational safety and health community collaboratively in nanotechnology research. ▪ http://www.cdc.gov/niosh/topics/nanotech/.
NIH	<ul style="list-style-type: none"> ▪ Through its research project grants and coordinated center programs, NIH supports extensive, fundamental research on nanomaterials and their biological interactions that broadly informs and supports EHS research. ▪ The National Cancer Institute established the Nanotechnology Characterization Laboratory (NCL) in collaboration with NIST and FDA to provide critical infrastructure and nanomaterials characterization services for cancer researchers. Progress includes: <ul style="list-style-type: none"> ○ Continued development of assays and methodologies to characterize nanoparticles' physical attributes, their <i>in vitro</i> biological properties, and their <i>in vivo</i> compatibility using animal models ○ Accelerated transition of basic nanoscale particles and devices into clinical applications ▪ National Institute of Environmental Health Sciences (NIEHS) continues to build an understanding of possible human health effects of nanomaterial exposure through multiple research efforts, including: <ul style="list-style-type: none"> ○ Funding of three research grants through a joint solicitation with EPA and NSF ○ Funding of five new extramural grants in 2007 ○ Initiation of the NanoHealth Enterprise, a partnership of NIH institutes, Federal agencies, and public and private partners to support research to address critical research needs for the safe development of nanoscale materials and devices ▪ The National Toxicology Program (NIEHS) through its Nanotechnology Safety Initiative continues research on: <ul style="list-style-type: none"> ○ Nonmedical, commercially relevant and available nanoscale materials to which humans are intentionally being exposed, such as cosmetics and sunscreens ○ Nanoscale materials representing specific classes such as fullerenes (buckyballs) and metal oxides so that information can be extrapolated to other members of those classes ○ Subsets of nanomaterials to test specific hypotheses about a key physiochemical parameter such as size, composition, shape, or surface chemistry ▪ http://www.becon.nih.gov/nano.htm.
NIST	<p>Nanotechnology is a research focus for NIST with a direct emphasis on innovation and traceable measurements to advance not only the development of standards for nanotechnology-enabled products and devices, but also the necessary national-scale measurement infrastructure to support the EHS aspects of nanomaterials. Specifically, NIST continues to:</p> <ul style="list-style-type: none"> ▪ Provide a scientific basis to the health and environmental effects of nanotechnology. ▪ Enable U.S. industry to safely develop, exploit, and commercialize nanotechnologies. ▪ Leverage nanotechnology standards development work among other Federal programs. ▪ Establish direct collaborations with other Federal agencies. ▪ Work with representatives from the risk assessment and regulatory communities represented by not only government, but also academia, industry, and the international community.

III. Framework for Addressing EHS Research Needs

Agency	Nano EHS Research, Activities, Plans, and Strategic Efforts (individual and joint)
	<ul style="list-style-type: none"> ▪ Work with standards development organizations. ▪ Collaborate with the National Cancer Institute's Nanotechnology Characterization Laboratory and the Food and Drug Administration on the development of a battery of characterization tools for preclinical evaluation of nanomaterials and devices intended for cancer therapeutics. ▪ Sponsor stakeholder-driven nanotechnology workshops and meetings. ▪ Develop methods for physical and chemical characterization of nanomaterials. ▪ Develop standard reference materials. ▪ http://www.nist.gov/nanoehs.
NSF	<p>NSF provides foundational knowledge, education, and infrastructure for EHS in support of nanotechnology and other agency missions. NSF-sponsored research addresses the three sources of nanostructured materials (natural, incidental, and manufactured) in different environmental settings (air, water, soil, biosystems, and the work environment), as well as the nonclinical biological implications. The programs are upstream, looking for the utilization, implications and mitigation of the effects of the current and new generations of nanomaterials. These topics are supported through programs in all research directorates. There are several EHS priorities for the societal dimensions of nanotechnology:</p> <ul style="list-style-type: none"> ▪ New measurement methods and instrumentation for nanoparticle characterization in air, soil, and water, for exposure rates, and for toxicity of nanomaterials. ▪ Transport phenomena of nanoscale aerosols and colloids, interaction of nanomaterials with cells and living tissues (human, animal, and plant). ▪ Physico-chemical-biological processes of nanostructures dispersed in the environment and at the workplace; develop models for predicting impact of nanomaterials on health and safety over the entire life cycle. ▪ Separation of nanoparticles from fluids, including water filtration. ▪ Safety of manufactured nanoparticles. ▪ Research on risk governance methods. ▪ Development of user facilities. ▪ Educational programs. <p>NSF has established an environmental component of this NNI investment since FY 2001 and now spends about 7% of the nanotechnology budget for this purpose. The NSF estimation for EHS is \$29.2 million (7.5% of NSF nanotechnology funding) in FY 2008, and \$30.6 million in the FY 2009 request (7.7% of the nanotechnology total). This includes a new multidisciplinary center in collaboration with EPA to conduct fundamental research on the environmental, health, and safety impacts of nanomaterials. This research will explore the interactions between nanoscale particles and materials and the living world with development of innovative methods of investigation and instrumentation.</p> <ul style="list-style-type: none"> ▪ http://www.nsf.gov/nano.
U.S. Army ERDC	<p>U.S. Army Engineer research and Development Center (ERDC) is leading the way to understand the unique environmental attributes of engineered nanomaterials used in military applications and potential changes in risk over the life cycle of nanotechnology-enabled products. Specifically, the ERDC Nanomaterials Risk Research Cluster is focusing on:</p> <ul style="list-style-type: none"> ▪ Advanced characterization of nanomaterial properties and risks for technology improvement and risk reduction.

III. Framework for Addressing EHS Research Needs

Agency	Nano EHS Research, Activities, Plans, and Strategic Efforts (individual and joint)
	<ul style="list-style-type: none"> ▪ Risk and decision analysis tools for prioritizing technology needs for product developers. ▪ Collaborations with commercial and governmental technology developers to address priority materials. ▪ Characterization of the fate and toxicology of engineered nanomaterials in environmental systems. ▪ Recognized leadership and advising role to the Office of the Secretary of Defense and the North Atlantic Treaty Organization (NATO).
USGS	<ul style="list-style-type: none"> ▪ Research activities of the Contaminant Biology Program and the Toxic Substances Hydrology Program focus on environmental occurrence, fate, and effects. ▪ USGS is in the planning phase for additional research on nanoparticles in the environment. ▪ Science on nanoparticles is a component of the recently published USGS Science Strategy, <i>Facing Tomorrow's Challenges—U.S. Geological Survey Science in the Decade 2007–2017</i>.

With the continued growth in EHS research, the NNI member agencies will need to be vigilant in promoting a consistent level of coordination across both the Federal Government and outside collaborators. In addition to the existing efforts of the NEHI Working Group and the bottom-up development of multiagency activities and research programs that address agency needs and the research priorities of the NNI, the implementation plans described in this document will help ensure a sustained level of coordination that is currently in place as nanotechnology-related EHS research continues to grow, both within and outside the Federal Government.

Given the early stage of nanomaterials development and their commercialization, as well as the expected increase in information and knowledge about potential risks, the NNI will need to periodically review and update its EHS research priorities. The workshops described above will provide input to such an update, which is anticipated to be necessary every 3-5 years. Furthermore, as part of the legislatively mandated review of the NNI by the President's Council of Advisors on Science and Technology and the National Academies, it is anticipated that the NNI EHS research strategy will receive independent review and oversight of coordination, progress, implementation, and management in the appropriate context of the overall NNI interagency coordination through the NSET Subcommittee, its working groups, and the NNCO.

Appendix A. FY 2006 Nanotechnology-Related EHS Research Projects

This appendix provides information on the portfolio of Federally funded nanotechnology-related EHS research in FY 2006. Obtaining this data was one of the key steps used by the NSET Subcommittee to develop a strategy for the Federal Government to move forward in its approach to funding and conducting nanotechnology-related EHS research. In summary, the steps being used to develop a Federal Government strategy for nanotechnology-related EHS research are: (1) identifying priority research needs in the field of nanotechnology-related EHS research; (2) choosing the top 25 broad research needs for nanotechnology-related EHS research; (3) examining the portfolio of Federally funded nanotechnology-related EHS research; (4) identifying weaknesses and/or gaps in the Federal Government's nanotechnology-related EHS research; and (5) developing a strategy to address the weaknesses and/or gaps in the Federal Government portfolio. As an ongoing effort, the NSET Subcommittee will be periodically reviewing progress toward addressing identified needs and updating the research needs and priorities to take into consideration the introduction of new materials, new research discoveries, and advances made by entities other than U.S. Government-funded bodies.

In carrying out this step, all NNI member agencies that are funding nanotechnology R&D evaluated their FY 2006 portfolios in the areas of environmental, health, and safety research R&D for engineered nanoscale materials. To assist with this formative analysis of research programs, the Office of Management and Budget (OMB) issued a one-time call for the agencies to "select from your agency's nanotechnology R&D those FY 2006 projects that contribute to the five major categories of EHS R&D identified in the NNI EHS Research Needs document: (1) Instrumentation, Metrology, and Analytical Methods; (2) Nanomaterials and Human Health; (3) Nanomaterials and the Environment; (4) Human and Environmental Exposure Assessment; and (5) Risk Management Methods."

The research reported in response to this call is more extensive than what has been previously reported in the annual NNI supplements to the President's budget. EHS R&D funding reported under the previous Societal Dimensions Program Component Area (PCA) in the budget supplements is limited to efforts whose primary purpose is to understand and address potential risks to health and to the environment posed by nanotechnology. For the special OMB data call reported herein, agencies were asked to also include those portions of projects reported under other PCAs that are directly relevant to EHS research needs. This captures, for example, the development of instruments for environmental surveillance reported under the Instrumentation Research, Metrology, and Standards for Nanotechnology PCA. It also captures an appropriate portion of projects from the National Institutes of Health, which may include research on safety as part of a larger effort to develop health-related nanotechnology reported under other PCAs.

NSET Subcommittee and NEHI Working Group representatives worked with agency program staff to verify that each reported project was relevant to one or more of the five major EHS R&D categories. Programs with components relevant to more than one of the five research needs categories were subdivided whenever funding for an individual component exceeded \$50,000 and, at the reporting agency's discretion, for lesser amounts exceeding 10% of the program total. The respective components were then treated as individual projects. As the interagency group analyzed the results of the data call, projects were assigned both in terms of the kind of information developed (some information is of greater relevance to supporting risk management than others) and the appropriate sequencing of research (some research should be timed to occur following other research in order to gain the greatest benefit to risk management needs). Projects relevant to more than one category or need were assigned to the need that was primarily being addressed by the research. In a small number of cases, it was not possible to identify a single primary need; these were categorized as addressing "multiple" needs. In some cases, projects were related to the overarching

research category but did not align with any of the top five priority areas identified for a given category. These projects were categorized as addressing “other” needs.

In the use and analysis of these data to identify strength, weaknesses, or gaps with respect to the overarching research needs, the interagency group of experts considered carefully the following limitations of this snapshot of the growing nanotechnology EHS research program. Readers of this document should be equally mindful of these limitations:

- The data represent only research funded in FY 2006. Many projects are multiyear and therefore actual research associated with projects listed may have taken place in earlier or later years. However, projects begun after FY 2006 are not captured.
- Projects listed are prospective, that is they are planned research, not research results. Basic research projects may diverge from the original proposal, based on initial results or as other information becomes available.
- The list represents only Federally funded research. It does not include any research in these areas that is supported by industry, nonprofit organizations, or other governments.

The tables of nanotechnology-related EHS research projects that follow are grouped by research needs category, research need, funding agency, and type of funding (intramural, extramural, SBIR). They provide the following information, where relevant and informative, for each project:

- Index number: a unique identifier for each project, which may also be used to retrieve award abstracts and additional information on the project from the NNI website at <http://www.nano.gov/html/society/EHSprojects.html>
- Lead Institution: the institution of the lead principal investigator for the project
- Award ID: Grant, contract, or project number as assigned by the funding agency
- Project: the project title (or a brief description where no title was available)
- Notes: additional information to clarify why the project is relevant to the category and/or particular research need if the title or research topic description was not viewed as adequately descriptive

Funding accounted for in the projects in the table does not reflect the entire budget of the projects reviewed, but rather comprises the best-guess estimate provided by agency staff of the portion of the project targeted to EHS-relevant activity.

Instrumentation, Metrology, and Analytical Methods

No. of Projects: 36

Develop methods to detect nanomaterials in biological matrices, the environment, and the workplace

Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>NIH</u>	<u>Extramural</u>			
A1-1	A Study of Model Beta-cells In Diabetes Treatment	2R01DK047858-10A	University of Florida	This project will pave the way for further imaging studies in tissue engineering that may be applicable to the nanoscale.
http://www.nano.gov/html/society/EHSprojects.html#A1-1				
A1-3	Implantable 16-256 Channel Data System For Sleep In Mice	1R01MH071830-01A	Washington State University	In combination with other intracellular measurement techniques, which may involve nanoparticles like quantum dots, this technique will improve ways of correlating electrophysiological measurements with intracellular biochemical or genetic pathway measurements not currently done.
http://www.nano.gov/html/society/EHSprojects.html#A1-3				
A1-4	Power Harvesting In Implanted Neural Probes	1R21MH074703-01A	Johns Hopkins University	This research is in neural micro/nano systems within a biomedical instrumentation laboratory developing technologies for recording from neurons or the brain and developing interfaces, at molecular/cellular and at the systems level. Micro- and nanotechnology are utilized for the fabrication of sensors.
http://www.nano.gov/html/society/EHSprojects.html#A1-4				
A1-5	Surface Plasmon-coupled Fluorescence Microscope To Study Ion Channel Dynamics	1R21MH078822-01	University of Chicago	This work supports nano- to micro-scale fluorescence measurements of electric fields in molecules.
http://www.nano.gov/html/society/EHSprojects.html#A1-5				
A1-6	A Turnkey, Wireless, EEG/EMG/Biosensor Measurement	1R43MH076318-01	Pinnacle Technology, Inc.	In combination with other intracellular measurement techniques, which may involve nanoparticles like quantum dots, this technique will improve ways of correlating electrophysiological measurements with intracellular biochemical or genetic pathway measurements in ways not currently done.
http://www.nano.gov/html/society/EHSprojects.html#A1-6				
A1-7	Cut Nanotube Capsules For MR Imaging	5R21EB005390-02	TDA Research, Inc.	This project strives to improve magnetic resonance techniques for cellular and molecular imaging through the development of new contrast agents based on nanotubes and magnetic nanomaterials. Biocompatibility and physical characterization studies are central components.
http://www.nano.gov/html/society/EHSprojects.html#A1-7				
A1-8	Flourescent Ceramic Nanoprobes	5R21EB005365-02	Sandia National Laboratory	This effort to optimize the design, delivery, and imaging of the novel nanoprobes will lead to the development and improvement of methods to detect and characterize nanomaterials.
http://www.nano.gov/html/society/EHSprojects.html#A1-8				

Appendix A. FY 2006 Nanotechnology-Related EHS Research Projects

Abstract #	Project	Award ID	Lead Institution	Additional Notes
A1-9	Targeted MRI With Protein Cage Architectures	5R21EB005364-02	Montana State University	This project aims to achieve a one-order-of-magnitude increase in the ability to detect and image molecular level events in vitro and in vivo. Improvement to techniques for detecting nano-particle contrast agents supports metrology methods to detect nanomaterials.
http://www.nano.gov/html/society/EHSprojects.html#A1-9				
A1-10	MFe ₂ O ₄ -loaded Polymer Micelles As Ultra-sensitive MR Mo*	5R21EB005394-02	University of Texas-MD Anderson	This project targets the development of ultra-sensitive magnetic resonance imaging probes for cancer molecular imaging applications. To evaluate the safety, biocompatibility, and effectiveness of probe materials (which include nanostructured composites), new fundamental methods to detect and characterize the probe materials will be developed.
http://www.nano.gov/html/society/EHSprojects.html#A1-10				
A1-11	Membrane Topography of Cell Signaling Complexes	3P01DK060564-05S1	Univ of Massachusetts Medical School	This program project combines biochemical, structural and imaging approaches to study proteins by effectively combining diverse experimental techniques with powerful deconvolution algorithms to achieve resolution at the nanometer level.
http://www.nano.gov/html/society/EHSprojects.html#A1-11				
A1-12	Non-Viral Liver-targeted Gene Delivery	5R01DK068399-02	Johns Hopkins University	Project supports the synthesis and characterization of nanomaterials targeted for biological study. Nanomaterials are characterized at the tissular, cellular, and subcellular level by various techniques including electron microscopy.
http://www.nano.gov/html/society/EHSprojects.html#A1-12				
A1-13	Morphogen Gradients In Microfluidic Cultures	5R21MH075059-02	University of California-Irvine	In combination with other intracellular measurement techniques, which may involve nanoparticles like quantum dots, this technique will improve ways of correlating electrophysiological measurements with intracellular biochemical or genetic pathway measurements not currently done.
http://www.nano.gov/html/society/EHSprojects.html#A1-13				
NIH Intramural				
A1-2	Develop Fiber-Optic Confocal Microscope With Nanoscale Depth Resolution	1Z01HD000261-09	NICHD/SBSP	A critical element of this project is the development of methods and instrumentation to image tissues and study biological phenomena with nanoscale resolution.
http://www.nano.gov/html/society/EHSprojects.html#A1-2				
NIST Intramural				
A1-14	Single Photon Sources and Detectors		NIST	Single-photon spectroscopic techniques are being developed to assess the purity and chemical composition of nano-EHS relevant nanomaterials in complex matrices such as tissues or fluids.
http://www.nano.gov/html/society/EHSprojects.html#A1-14				
A1-15	Quantum Optical Metrology		NIST	This project will impact the development of rapid spectroscopic techniques for detecting chemical and biological agents. Such work furthers the ability to detect nanomaterials.
http://www.nano.gov/html/society/EHSprojects.html#A1-15				

Appendix A. FY 2006 Nanotechnology-Related EHS Research Projects

Abstract #	Project	Award ID	Lead Institution	Additional Notes
A1-16	Nano-scale Engineered Sensors for Ultra-low Magnetic Field Metrology		NIST	New measurement approaches to study novel nanostructured material are a principle component of this project, and support the development of methods to detect nanomaterials.
				http://www.nano.gov/html/society/EHSprojects.html#A1-16
A1-17	Superresolution, In Situ Microscopies for Characterization of Nanostructured Materials		NIST	This project seeks to develop a superresolution optical microscopy platform. This will enable in-situ characterization of organic and biological materials and supports the development of methods to detect nanomaterials.
				http://www.nano.gov/html/society/EHSprojects.html#A1-17
A1-18	Metrology of Semiconductor Quantum Nanowires		NIST	This project investigates use of semiconductor quantum nanowires in a variety of sectors. Metrology efforts support the development of methods to detect nanomaterials.
				http://www.nano.gov/html/society/EHSprojects.html#A1-18
A1-19	High Throughput Hyperspectral Data Analysis		NIST	This project is developing new techniques for rapid acquisition of chemical information with high spatial resolution.
				http://www.nano.gov/html/society/EHSprojects.html#A1-19
A1-20	Dimensional Metrology Program		NIST	A wide range of ion, electron, and X-ray spectroscopies, microscopies, and microanalysis techniques are under exploration for the detection and characterization of nanomaterials.
				http://www.nano.gov/html/society/EHSprojects.html#A1-20
A1-21	Surface Metrology		NIST	This program supports the development of calibration techniques which will allow accurate detection and measurement of nanomaterials.
				http://www.nano.gov/html/society/EHSprojects.html#A1-21
A1-22	Phase Sensitive Scatterfield Imaging for Sub-10 nm Dimensional Metrology		NIST	Investigations on the possible optical measurements of nanometer-sized features supports the development of methods to detect nanomaterials.
				http://www.nano.gov/html/society/EHSprojects.html#A1-22
A1-23	Metrology for the "Fate" of Nanoparticles in Biosystems		NIST	This project seeks to develop a comprehensive set of metrological tools for measuring nanoparticles in biomaterials and bio-relevant media.
				http://www.nano.gov/html/society/EHSprojects.html#A1-23
NSF	Extramural			
A1-24	SST - Ferroelectric Thin-film Active Sensor Arrays For Structural Health Monitoring	0528873	University South Carolina	The advancement of nano investigative techniques (including a range of microscopy techniques) are a critical component of this project.
				http://www.nano.gov/html/society/EHSprojects.html#A1-24

Appendix A. FY 2006 Nanotechnology-Related EHS Research Projects

Abstract #	Project	Award ID	Lead Institution	Additional Notes
A1-25	CAREER: Hybrid Nanomaterials For Multi-functional Sensors - Synthesis and Characterization of Nanocomposite Thin-films For Device Applications http://www.nano.gov/html/society/EHSprojects.html#A1-25	0547273	Duke University	Metrology efforts support the development or improvement of methods to detect nanomaterials.
A1-26	CAREER: Integrated Research and Education In Nano and Microscale Photoacoustic and Photothermal Microscopy http://www.nano.gov/html/society/EHSprojects.html#A1-26	0448796	Boston University	Metrology efforts support the development or improvement of methods to detect nanomaterials.
A1-27	REU Site For Nanoscale Structures and Integrated Biosensors http://www.nano.gov/html/society/EHSprojects.html#A1-27	0552772	Wayne State University	Metrology efforts support the development or improvement of methods to detect nanomaterials.
A1-28	Selective Filling of Nanostructured Packings For Chromatographic Chip Systems http://www.nano.gov/html/society/EHSprojects.html#A1-28	0522656	Rensselaer Polytechnic Institute	This work is aimed at developing a highly efficient chromatographic chip system able to separate nanoparticles, detect the presence of nanoparticles, and prepare samples by particle size for further chemical and biological characterization.
A1-29	NSEC: Center For Molecular Function At the Nanoscale http://www.nano.gov/html/society/EHSprojects.html#A1-29	0425780	University of Pennsylvania	This work is targeted at developing new instrumentation for detection and characterization of nanoparticles in biosystems.
A1-30	National High Magnetic Field Laboratory http://www.nano.gov/html/society/EHSprojects.html#A1-30	0084173	Florida State University	Metrology efforts support the development or improvement of methods to detect nanomaterials.
A1-31	IGERT: Nanoparticle Science and Engineering http://www.nano.gov/html/society/EHSprojects.html#A1-31	0114372	University of Minnesota-Twin Cities	Metrology efforts support the development or improvement of methods to detect nanomaterials.
A1-32	Molecular Simulation of Chemical Warfare Agent Adsorption http://www.nano.gov/html/society/EHSprojects.html#A1-32	0522005	Wayne State University	Efforts targeted to investigation and design of nanostructured molecular sieves using molecular and atomistic simulation for detection of toxic industrial materials at the nanoscale or molecular level.
A1-33	NSEC: Network For Hierarchical Manufacturing http://www.nano.gov/html/society/EHSprojects.html#A1-33	0531171	University of Massachusetts-Amherst	Metrology efforts support the development or improvement of methods to detect nanomaterials.
A1-34	NSEC: Nanoscale Science & Engineering Center for Integrated Nanopatterning and Detection Technologies http://www.nano.gov/html/society/EHSprojects.html#A1-34	0118025	Northwestern University	These efforts aim to develop state-of-the-art instrumentation for detection of nanoparticles with high accuracy and sensitivity.

Abstract #	Project	Award ID	Lead Institution	Additional Notes
A1-35	CAREER: Engineering Nucleic Acid Devices	0448835	California Institute of Technology	This work is targeted toward understanding and developing new principles and toward the construction of versatile and inexpensive biosensors with nanoscale sensitivity.
http://www.nano.gov/html/society/EHSprojects.html#A1-35				
A1-36	NSEC: Center of Integrated Nanomechanical Systems	0425914	University of California-Berkeley	Projects are targeted to the development and use of two closely related nanosensor systems: (1) a new personal and community-based sensor for the environmental monitoring of nanoparticles, and (2) technology for the chemical/biological sensing of nanoparticles with integrated communication and power for tagging, tracking, and locating applications.
http://www.nano.gov/html/society/EHSprojects.html#A1-36				

No. of Projects: 14 *Understand how chemical and physical modifications affect the properties of nanomaterials*

Abstract #	Project	Award ID	Lead Institution	Additional Notes
DOE		Extramural		
A2-1	Single Molecule Fluorescence In Nanoscale Environments		University of Rochester	This project seeks to understand nanoscale material optical phenomena through the detection of a single molecule in a complex environment. This work provides a basis for the development of novel schemes and techniques for molecular identification and analysis, and supports efforts to understand nanomaterial structures, properties and behavior.
http://www.nano.gov/html/society/EHSprojects.html#A2-1				
A2-2	The Reaction Specificity of Nano Particles In Solutions		Pacific Northwest National Laboratory	This is fundamental research directed toward understanding and controlling the chemical properties of nanomaterials. The goal is to understand the mechanism responsible for the overall particle reactivity and reaction selectivity of reactive metal and oxide nanoparticles. This supports efforts to further understand nanomaterial structures, behaviors, and modifications.
http://www.nano.gov/html/society/EHSprojects.html#A2-2				
A2-3	Manipulation and Quantitative Interrogation of Nanostructures		Lawrence Livermore National Laboratory	This program supports a quantitative investigation of the effects of different parameters on the properties of nanoparticles and enables a better understanding of the behavior of nanomaterials as a function of their physical properties.
http://www.nano.gov/html/society/EHSprojects.html#A2-3				
A2-4	Diffraction Studies of Glasses, Liquids, and Nanoclusters		University of Houston	This project supports work on the the determination of the structure of nanophase clusters. Metrology efforts under investigation provide developments or improvements to methods to understand the interaction of modifications with properties of nanomaterials, a focus for this research need.
http://www.nano.gov/html/society/EHSprojects.html#A2-4				

Appendix A. FY 2006 Nanotechnology-Related EHS Research Projects

Abstract #	Project	Award ID	Lead Institution	Additional Notes
A2-5	New Methods and Instrumentation For the Study of Complex Magnetic Materials and Nanostructures Using Soft X-ray Spectroscopies		University of Tennessee	This project supports development and deployment of new methods and instrumentation to study nanomaterials and nanostructures. The advanced tools may further the ability to measure properties of complex materials in relation to structures of other features.
http://www.nano.gov/html/society/EHSprojects.html#A2-5				
A2-6	Using Plasmon Peaks In Electron Energy-Loss Spectroscopy To Determine the Physical and Mechanical Properties of Nanoscale Materials		University of Virginia	This project seeks to provide instrumentation to routinely determine the mechanical (and physical) properties of nanoscale materials. Application of the technique to a number of model experimental systems and situations will further efforts to better understand the effects of modifications on the physical properties of nanomaterials.
http://www.nano.gov/html/society/EHSprojects.html#A2-6				
A2-7	Nano-structures Examined With Spin-polarized Positron Beams		Washington State University	This project supports the examination of nano-structures and their properties using novel instrumentation, which may ultimately provide new avenues to investigate how modifications affect nanomaterial properties.
http://www.nano.gov/html/society/EHSprojects.html#A2-7				
NIH		Extramural		
A2-8	Project 6: Use of Oxidants Produced By Nanoparticulate & Granular Zero-Valent Iron	3P42ES004705-19S1	University of California-Berkeley	This project provides insight into the processes occurring on or near ZVI surfaces by using techniques designed to probe the surface, such as potentiometry, surface-enhanced Raman spectroscopy and electrochemical quartz microbalance methods.
http://www.nano.gov/html/society/EHSprojects.html#A2-8				
A2-9	Bladder Tissue Engineering Through Nanotechnology	5R21DK072450-02	Northwestern University	This project studies the effects of modifications of materials under study, with an application focus.
http://www.nano.gov/html/society/EHSprojects.html#A2-9				
A2-10	Nano-Porous Alumina Membranes For Enhanced Hemodialysis Performance	1R41DK074254-01	EMV Technologies, LLC	The new kidney dialysis membranes under study in this project will be characterized for parameters including those that affect the chemical or physical properties of the material. These metrology efforts support the ability to understand the effects of modifications to nanomaterials on their properties.
http://www.nano.gov/html/society/EHSprojects.html#A2-10				
A2-11	Biotechnology Research Infrastructure At ASU - Investigation of Aggregation On Thin Films For Gold Nanoparticles and Nanorods	5P20MD001085-02	Albany State University	This project supports efforts to understand and characterize nanoparticle surfaces and modifications to such surfaces by using nanotechnology to develop the basic science of nanoparticle thin films.
http://www.nano.gov/html/society/EHSprojects.html#A2-11				
NIST		Intramural		

Abstract #	Project	Award ID	Lead Institution	Additional Notes
A2-12	Theoretical Models of Chemical Properties of Nanostructures		NIST	This program supports investigations which seek to understand the biological or environmental response of a nanomaterial to changes in a defined set of physical parameters.
http://www.nano.gov/html/society/EHSprojects.html#A2-12				
A2-13	Nanocharacterization - NCI		NIST	Nanomaterial characterizations of direct relevance to the standardization of toxicology protocols are an integral component of this program.
http://www.nano.gov/html/society/EHSprojects.html#A2-13				
A2-14	Metrology for Tissue Engineering; Test Patterns and Cell Function Indicators		NIST	This program seeks to provide measurement tools for tissue engineering research. High-throughput and combinatorial methods for characterizing biomaterials and screening cell-material interactions are large areas of investigation.
http://www.nano.gov/html/society/EHSprojects.html#A2-14				
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No. of Projects: 4	<i>Develop methods for standardizing assessment of particle size, size distribution, shape, structure, and surface area</i>			
Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>DOE</u>	<u>Extramural</u>			
A3-1	A Fundamental Study of Transport Within A Single Nanoscopic Channel		University of Texas	Quantification of mass transport through single-nanopore models having well-defined structures is important to understanding process of technological and environmental significance, and supports the development of methods for the determination of particle size.
http://www.nano.gov/html/society/EHSprojects.html#A3-1				
<u>NIOSH</u>	<u>Extramural</u>			
A3-2	Monitoring and Characterizing Airborne Carbon Nanotube Particles	1R01OH008807-01	New York University School of Medicine	
http://www.nano.gov/html/society/EHSprojects.html#A3-2				
<u>NIST</u>	<u>Extramural</u>			
A3-3	Nanoparticle Risk Impact and Assessment Program		NIST	This program supports the development of techniques to monitor and characterize airborne nanoparticles.
http://www.nano.gov/html/society/EHSprojects.html#A3-3				
<u>NSF</u>	<u>Extramural</u>			
A3-4	IMR: Development of An Analyzer For Size and Charge Characterization of Nanoparticles In Research and Training	0526977	University of Arkansas Little Rock	This effort is directed toward the development of an instrument to study the properties of minute-sized airborne particles.
http://www.nano.gov/html/society/EHSprojects.html#A3-4				
<hr/>				
No. of Projects: 6	<i>Develop certified reference materials for chemical and physical characterization of nanomaterials</i>			

Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>NIH</u> <u>Extramural</u>				
A4-1	Cryopreservation of Tissue Engineered Substitutes	1R01DK073991-01A	Georgia Institute of Technology	This project focuses on the development of tissue engineered substitutes with an emphasis on understanding the effects of cryopreservation on cells and biomaterials. This is critical groundwork for the development of cell- or bio-based reference materials.
http://www.nano.gov/html/society/EHSprojects.html#A4-1				
<u>NIH</u> <u>SBIR</u>				
A4-2	Submicron Particles and Fibers For Toxicological Studies	5R43ES013367-02	LNKChemSolutions	This research is dedicated to the manufacturing of nanoparticles for toxicology research. Such research supports the development of standard materials and standardized toxicological testing protocols.
http://www.nano.gov/html/society/EHSprojects.html#A4-2				
<u>NIST</u> <u>Intramural</u>				
A4-3	R&D For Carbon Nanotube Reference Materials		NIST	This program targets the development of specific reference materials for nanomaterials.
http://www.nano.gov/html/society/EHSprojects.html#A4-3				
A4-4	R&D For Nanoparticle (non-Carbon Nanotube) Reference Materials		NIST	This program targets the development of specific reference materials for nanomaterials.
http://www.nano.gov/html/society/EHSprojects.html#A4-4				
A4-5	Fundamental Metrology for Carbon Nanotube Science and Technology		NIST	This program targets the development of specific reference materials for nanomaterials.
http://www.nano.gov/html/society/EHSprojects.html#A4-5				
A4-6	Scanning Probe Microscopy Reference Specimens		NIST	This program targets the development of specific reference materials for nanometrology via scanning probe microscopy (SPM).
http://www.nano.gov/html/society/EHSprojects.html#A4-6				
No. of Projects: 15	<i>Develop methods to characterize a nanomaterial's spatio-chemical composition, purity, and heterogeneity</i>			
Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>DOE</u> <u>Extramural</u>				
A5-1	Chemical Analysis of Nanodomains		Ames Laboratory	This program seeks the development of new methodologies to advance mapping of surfaces in the nanoscale environment.
http://www.nano.gov/html/society/EHSprojects.html#A5-1				
A5-2	Atomic Scale Chemical Imaging In 3 Dimensions		Argonne National Laboratory	This program supports the development of advanced electron microcopies for atomic scale characterization of spatio-chemical composition.
http://www.nano.gov/html/society/EHSprojects.html#A5-2				

Appendix A. FY 2006 Nanotechnology-Related EHS Research Projects

Abstract #	Project	Award ID	Lead Institution	Additional Notes
A5-3	Directed Energy Interactions With Surfaces		Argonne National Laboratory	This effort explores the interactions of energetic particles with nanoscale surfaces. Analysis of such information can provide mass-based analysis of nanomaterial and detailed information on trace-level impurities.
http://www.nano.gov/html/society/EHSprojects.html#A5-3				
A5-4	Studies of Nanoscale Structure and Structural Defects of Advanced Materials		Brookhaven National Laboratory	This work will document property-sensitive nanoscale structure and defects of materials through a combination of experiment, modeling, and simulations.
http://www.nano.gov/html/society/EHSprojects.html#A5-4				
A5-5	Microscopy Investigations of Nanostructured Materials		Lawrence Berkeley National Laboratory	This program aims to develop novel microscopies for the analysis of nanostructured materials, including methods for assessing purity and heterogeneity of nanomaterials.
http://www.nano.gov/html/society/EHSprojects.html#A5-5				
A5-6	Three-dimensional Imaging of Nanoscale Materials By Using Coherent X-rays		University of California-Los Angeles	This program supports the development of methods to determine the 3D structures of single particles down to the atomic level.
http://www.nano.gov/html/society/EHSprojects.html#A5-6				
A5-7	Electron Diffraction Determination of Nanoscale Structures		Harvard University	These structural studies support the development of methods to assess dimensional and chemical properties of nanomaterials.
http://www.nano.gov/html/society/EHSprojects.html#A5-7				
A5-8	Quantitative Electron Nano-crystallography and Nano-spectroscopy		University of Illinois-Urbana-Champaign	This programs seeks to develop techniques to determine the structures of individual nanostructures and complex crystals, ultimately with atomic resolution in three dimensions.
http://www.nano.gov/html/society/EHSprojects.html#A5-8				
A5-9	High Resolution Lenseless 3d Imaging of Nanostructures With Coherent X-rays		Stony Brook University	This work will improve and standardize data and image handling for techniques three dimensional imaging of nanostructures.
http://www.nano.gov/html/society/EHSprojects.html#A5-9				
NIH Extramural				
A5-10	Thin-walled Micromolding	1R43DK074237-01	Miniature Tool And Die	This project measures flow in nano-volumes, furthering the evaluation of the physical properties of materials at the nanoscale, to support metrology needs and the development of methods to characterize a material's composition, purity, or heterogeneity.
http://www.nano.gov/html/society/EHSprojects.html#A5-10				
NIST Intramural				
A5-11	3-D Chemical Imaging at the Nanoscale		NIST	This development of methods to determine the distribution of chemical species in three dimensions directly supports this research need.
http://www.nano.gov/html/society/EHSprojects.html#A5-11				

Abstract #	Project	Award ID	Lead Institution	Additional Notes
A5-12	Metrology for the Manufacture of Robust Nanostructures		NIST	Measurement tools are being developed to characterize size, shape, molecular orientation, defect structure, and the elastic or anelastic properties needed to determine the stability of model nanostructures.
http://www.nano.gov/html/society/EHSprojects.html#A5-12				
NSF	Extramural			
A5-13	CAREER: Multi-scale and Multi-disciplinary Aspects of Indentation	0449268	SUNY at Stony Brook	This work is targeted to obtaining small samples from the surface of nanostructured materials or nanostructured particles in order to characterize them and obtain spatial distribution of the nanomaterial properties.
http://www.nano.gov/html/society/EHSprojects.html#A5-13				
A5-14	Acquisition of A Powder X-ray Diffractometer For Environmental and Materials Research At UC Merced	0619398	University of California-Merced	This diffractometer will be used for qualitative and quantitative phase identification, amorphous/crystalline characterization, polymorph discrimination, and impurity analysis in environmental and materials research, including further development of methods to study nanoparticles and their properties.
http://www.nano.gov/html/society/EHSprojects.html#A5-14				
A5-15	Engineering Research Center For Extreme Ultraviolet Science and Technology	0310717	Colorado State University	This project focuses on the goal of making EUV light, now mostly limited to a handful of large national facilities, available routinely in a broad variety of laboratory settings, for applications such as high-resolution imaging, spectroscopy, elemental- and bio-microscopy, and nano-fabrication.
http://www.nano.gov/html/society/EHSprojects.html#A5-15				

No. of Projects: 2

Addresses Multiple Research Needs In Instrumentation, Metrology, and Analytical Methods

Abstract #	Project	Award ID	Lead Institution	Additional Notes
NSF	Extramural			
A6-1	EPSCOR: Idaho Research Infrastructure Improvement	0447689	University of Idaho	This project includes work to develop and use nanosensors in aqueous environmental settings. Metrology efforts in the development of these sensors support characterizations of nanomaterials and assessment of their chemical and physical properties.
http://www.nano.gov/html/society/EHSprojects.html#A6-1				
A6-2	National Nanotechnology Infrastructure Network	0335765	Cornell University	This award supports a distributed, multi-faceted, and broadly accessible infrastructure that is being utilized in the development of instrumentation, metrology, and analytical methods to assess EHS aspects of nanomaterials.
http://www.nano.gov/html/society/EHSprojects.html#A6-2				

No. of Projects: 1

Addresses Research Needs In Instrumentation, Metrology, and Analytical Methods Not Captured in Priority Needs 1-5

Abstract #	Project	Award ID	Lead Institution	Additional Notes
NSF	Extramural			

Abstract #	Project	Award ID	Lead Institution	Additional Notes
A7-1	SGER: MEMS-based Preconcentrators With Nano-structured Adsorbents For Micro Gas Chromatography	0610213	Virginia Polytechnic Institute And State University	This is an application of nanomaterials for improving measurements in environmental and occupational safety. Specific work aims to develop higher performance sorbents for gas chromatography through the use of nanostructured thin films.
http://www.nano.gov/html/society/EHSprojects.html#A7-1				

Nanomaterials and Human Health

Understand the absorption and transport of nanomaterials throughout the human body

No. of Projects: 30

Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>DOD (AFOSR)</u> <u>Extramural</u>				
B1-1	Multidisciplinary University Research Initiative: Effect of Nanoscale Materials On Biological Systems: Relationship Between Physicochemical Properties and Toxicological Properties			
http://www.nano.gov/html/society/EHSprojects.html#B1-1				
<u>EPA</u> <u>Extramural</u>				
B1-2	Impact of Physicochemical Properties On Skin Absorption of Manufactured Nanomaterials	R833328	North Carolina State University	
http://www.nano.gov/html/society/EHSprojects.html#B1-2				
<u>NIH</u> <u>Extramural</u>				
B1-3	Nanoparticle, Raman-based Fiber-optic Glucose Sensor	5R33DK066990-03	Northwestern University	This grant will provide data on the implantation of noble metal nanoparticles in the skin.
http://www.nano.gov/html/society/EHSprojects.html#B1-3				
B1-4	Design of Targeting Enhancement for Drug Delivery	5R21CA112436-02	Case Western Reserve University	The EHS component of this proposal is to apply a combined theoretical and experimental approach to gain fundamental understanding of the physical principles of targeting by complex polymer nanoparticles by supplying an experimental practitioner with specific recommendations concerning the grafting density, PEG chain length, architecture, nanoparticle size and density of functional groups that ensure effective targeting of nanoparticles.
http://www.nano.gov/html/society/EHSprojects.html#B1-4				

Appendix A. FY 2006 Nanotechnology-Related EHS Research Projects

Abstract #	Project	Award ID	Lead Institution	Additional Notes
B1-5	Nanoparticles for Efficient Delivery To Solid Tumors	5R21CA114143-02	University of Washington	The goal of this research is to harness forces generated by actin polymerization to propel nanoparticles within the interstitial space by energy-mediated, cell-to-cell transfer, thus resulting in more efficient nanoparticle penetration. The EHS-relevant component of this research will demonstrate modifications that produce efficient delivery systems.
http://www.nano.gov/html/society/EHSprojects.html#B1-5				
B1-6	Engineered Intelligent Micelle for Tumor pH Targeting	5R01CA101850-04	University of Utah	The primary purpose of this research is to engineer functional polymeric micelles which target solid tumors in acidic extracellular fluid and utilize acidic endosome to treat sensitive and multidrug resistant tumors by designing biodegradable polymers sensitive to tumor acidity and to engineer polymeric micelles with or without targeting moiety that can truly recognize tumor pH or endosomal pH for triggered release, while keeping a minimal release rate during circulation.
http://www.nano.gov/html/society/EHSprojects.html#B1-6				
B1-7	Carolina Center of Cancer Nanotechnology Excellence	5U54CA119343-02	University of North Carolina-Chapel Hill	This project will bring together nano-particle engineering with the understanding/treatment of cancer for the delivery of therapeutic, detection and imaging agents for the diagnosis and treatment of cancer by fabricating "smart" functional particles for studies and evaluations. This will allow the fabrication of nano-biomaterials to accelerate translational understanding, detection and treatment of cancer.
http://www.nano.gov/html/society/EHSprojects.html#B1-7				
B1-8	Center of Nanotechnology for Treatment, Understanding, and Monitoring of Cancer	5U54CA119335-02	University of California-San Diego	This project seeks to develop a multi-functional platform that delivers payloads of both nanosensors and therapeutics directly to a tumor. The EHS-relevant component project focuses on the production of tumor-targeted, non-toxic nanoparticles
http://www.nano.gov/html/society/EHSprojects.html#B1-8				
B1-9	Emory-Georgia Tech Nanotechnology Center for Personalized and Predictive Oncology	5U54CA119338-02	Emory University	This EHS component of this research integrates nanotechnology with cancer biomolecular signatures and will provide data on the interaction of nanomaterials with cells.
http://www.nano.gov/html/society/EHSprojects.html#B1-9				
B1-10	Nanomaterials for Cancer Diagnostics and Therapeutics	5U54CA119341-02	Northwestern University	This project involves the use of nanomaterials in living systems and the evaluation of the biocompatibility and biodistribution of materials in the body and within cells.
http://www.nano.gov/html/society/EHSprojects.html#B1-10				
B1-11	The MIT-Harvard Center of Cancer Nanotechnology Excellence	5U54CA119349-02	Massachusetts Institute of Technology	This grant has a Toxicity Core and a Mouse Models Core that will provide in vivo information about nanomaterials behavior in model systems.
http://www.nano.gov/html/society/EHSprojects.html#B1-11				

Appendix A. FY 2006 Nanotechnology-Related EHS Research Projects

Abstract #	Project	Award ID	Lead Institution	Additional Notes
B1-12	The Siteman Center of Cancer Nanotechnology Excellence	5U54CA119342-02	Washington University	The goal of this project is to employ nanoparticles for targeted delivery of chemotherapeutic agents and for imaging. The EHS-relevant component is the mechanistic understanding of nanoparticle uptake and cell interaction. http://www.nano.gov/html/society/EHSprojects.html#B1-12
B1-13	Stanford Center of Cancer Nanotechnology Excellence	1U54CA119367-01	Stanford University	The goal of this project is to employ nanoparticles for imaging. The EHS-relevant component is the mechanistic understanding of nanoparticle uptake and cell interaction. http://www.nano.gov/html/society/EHSprojects.html#B1-13
B1-14	DNA-linked Dendrimer Nanoparticle Systems for Cancer Diagnosis	5R01CA119409-02	University of Michigan-Ann Arbor	The goal of this project is to employ dendrimer modules linked by oligonucleotides for targeted delivery of chemotherapeutic agents and for imaging. The EHS-relevant component is the mechanistic understanding of nanoparticle uptake and cell interaction. http://www.nano.gov/html/society/EHSprojects.html#B1-14
B1-15	Nanotherapeutic Strategy for Multidrug Resistant Tumors	5R01CA119617-02	Northeastern University	The study seeks to overcome multi-drug resistance in chemotherapy via a multifunctional approach to optimize delivery of pro-apoptotic drugs. The EHS-relevant component of the study will develop, characterize, and optimize long-circulating, biodegradable polymeric nanocarriers and evaluate the uptake, distribution, and intracellular concentrations of carried drugs. http://www.nano.gov/html/society/EHSprojects.html#B1-15
B1-16	Near-Infrared Fluorescence Nanoparticles for Targeted O*	5R01CA119387-02	University of Texas-MD Anderson	The goal of this project is to develop novel nanoparticles for molecular optical imaging applications for human cancers by establishing the effect of particle characteristics on the pharmacokinetics, biodistribution, clearance, extravasation, and intratumoral distribution of the nanoparticles. http://www.nano.gov/html/society/EHSprojects.html#B1-16
B1-17	Polymer Chelate Conjugates for Diagnostic Cancer Imaging	5R01CA097465-03	University of Utah	The goal of this project is to employ gadolinium nanoparticles for targeted delivery of chemotherapeutic agents and for imaging. The EHS-relevant component is the mechanistic understanding of nanoparticle biodistribution and clearance. http://www.nano.gov/html/society/EHSprojects.html#B1-17
B1-18	NIR Absorbing Nanoparticles for Cancer Therapy	1R21CA118778-01	Rice University	This grant will evaluate biodistribution, biocompatibility and tumor ablation efficacy of these NIR-absorbing nanoparticles. http://www.nano.gov/html/society/EHSprojects.html#B1-18
B1-19	A Tumor-specific Nanoimmunocomplex Markedly Improves Mr Imaging	1R41CA121453-01	Synergene Therapeutics, Inc.	The EHS component will better characterizenano-immuno-liposomesin animal models, determine optimized dose, optimal time to imaging, and perform toxicity studies in mice. http://www.nano.gov/html/society/EHSprojects.html#B1-19

Appendix A. FY 2006 Nanotechnology-Related EHS Research Projects

Abstract #	Project	Award ID	Lead Institution	Additional Notes
B1-20	In Vivo Imaging of Diabetogenic Cytotoxic T-lymphocytes	5R01DK064850-04	Massachusetts General Hospital	The goal of this project is to use iron oxide nanoparticles for enhanced MR imaging. The EHS-relevant component of this research is the mechanistic understanding of cell uptake of nanoparticles.
http://www.nano.gov/html/society/EHSprojects.html#B1-20				
B1-21	Imaging Tumor Blood Vessels In Bone Metastases From Breast Cancer	5R01DK067683-04	University of Texas-MD Anderson	The goal of this project is to use nanoshells for enhanced MR imaging. The EHS-relevant component of this research is the mechanistic understanding of cell uptake of nanoparticles.
http://www.nano.gov/html/society/EHSprojects.html#B1-21				
B1-23	CNS Gene Delivery and Imaging In Brain Tumor Therapy; Using Viral-sized Nanoparticles As A Model for Virus Particle Uptake	5R01NS034608-10	Oregon Health And Science University	The goal of this project is to use iron oxide nanoparticles for enhanced MR imaging. The EHS-relevant component of this research is the mechanistic understanding of influx and uptake of nanoparticles to the brain.
http://www.nano.gov/html/society/EHSprojects.html#B1-23				
B1-24	Nanoparticles for Sirna Delivery To Mammalian Neurons; Designing Nanoparticles That Will Move Through the CNS	5R21NS052030-02	University of Washington	The EHS component will characterise the interaction of nanoparticles with neurons.
http://www.nano.gov/html/society/EHSprojects.html#B1-24				
B1-25	Bioengineering of the Blood-Brain Barrier Permeability; Development, Characterization, and Use of Nanogel Carriers Through the BBB	5R01NS050660-02	University of Nebraska Medical Center	The goal of this project is to use Nanogel for targeted drug delivery across the blood/brain barrier. The EHS-relevant component of this research is the mechanistic understanding of brain uptake of nanoparticles.
http://www.nano.gov/html/society/EHSprojects.html#B1-25				
B1-26	Genotoxic Potential of Mixed Dust Exposures	5P42ES013660-0300	Brown University	Studies of mixed dust including inert and metal-bearing nanoparticles will aid in the development of rapid screens for toxic dusts.
http://www.nano.gov/html/society/EHSprojects.html#B1-26				
B1-30	Integrated Nanosystems for Diagnosis and Therapy	5U01HL080729-03	Washington University	The animal core in this center will perform a systematic review of chain lengths and branching, as well as composition of polymer-based structures, including biodistribution and excretion.
http://www.nano.gov/html/society/EHSprojects.html#B1-30				
NIH <u>Intramural</u>				
B1-22	Early Detection of Renal Injury	1Z01DK043400-07		The EHS component of this project is the mechanistic understanding of nanoparticle uptake, distribution, and clearance by using gadolinium nanoparticles for imaging. The EHS-relevant component of this research is
http://www.nano.gov/html/society/EHSprojects.html#B1-22				
NSF <u>Extramural</u>				
B1-27	Lung Deposition of Highly Agglomerated Nanoparticles	0646507	University of Minnesota-Twin Cities	
http://www.nano.gov/html/society/EHSprojects.html#B1-27				

Abstract #	Project	Award ID	Lead Institution	Additional Notes
B1-28	SGER: Nanostructured Interfaces for Targeted Drug Delivery	0553682	University of Minnesota-Twin Cities	This NSF project contains funding aimed at understanding and designing nanostructured interfaces for drug delivery targeting that specifically binds to infection or inflammation sites in human body. This engineered formulations of fractalkine-targeted stealth liposomes, their transport properties and binding capabilities will be evaluated in vitro.
http://www.nano.gov/html/society/EHSprojects.html#B1-28				

B1-29	Materials World Network: Designer Nanodiamonds for Detoxification	0602906	North Carolina State University
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<http://www.nano.gov/html/society/EHSprojects.html#B1-29>

No. of Projects: 13

Develop methods to quantify and characterize exposure to nanomaterials and characterize nanomaterials in biological matrices

Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>NIH</u>		<u>Extramural</u>		
B2-1	Multifunctional Nanoparticles for Intracellular Delivery	5R01CA098194-04	North Carolina State University	
http://www.nano.gov/html/society/EHSprojects.html#B2-1				
B2-2	Local Anesthetic Cardiotoxicity: Nanotechnology Therapy	5R01GM063679-04	University of Florida	
http://www.nano.gov/html/society/EHSprojects.html#B2-2				
B2-3	Bioabsorbable Membranes for Prevention of Adhesions	5R44GM063283-04	SUNY at Stony Brook	This EHS component of this grant focuses on developing anti-adhesion nanostructured products that reduce the formation of internal adhesions after surgery by assaying for biocompatibility of these nanostructured products using in vitro methods.
http://www.nano.gov/html/society/EHSprojects.html#B2-3				
B2-4	Nanomedex Propofol Microemulsions: Preclinical Studies To Fda Ind Application	2R44GM072142-02	Nanomedex, Inc	The goal of this grant is to make a nanoparticle-based emulsion of the propofol, a widely used anesthetic. The EHS-relevant component of this research is to determine the pharmacokinetic effects and biocompatibility properties of this emulsion using in vivo model systems.
http://www.nano.gov/html/society/EHSprojects.html#B2-4				
B2-5	Physicochemical Characterisation and Formulation of Fullerene C60 and Titanium Dioxide			
http://www.nano.gov/html/society/EHSprojects.html#B2-5				
<u>NIOSH</u>		<u>Extramural</u>		
B2-6	Role of Surface Chemistry In the Toxicological Properties of Manufactured Nanoparticles	1R01OH009141-01	Ohio State University	
http://www.nano.gov/html/society/EHSprojects.html#B2-6				
<u>NIOSH</u>		<u>Intramural</u>		

Abstract #	Project	Award ID	Lead Institution	Additional Notes
B2-7	Particle Surface Area As A Dose Metric		NIOSH/HELD	
http://www.nano.gov/html/society/EHSprojects.html#B2-7				
B2-8	Nanoparticles: Lung Dosimetry and Risk Assessment		NIOSH/EID	
http://www.nano.gov/html/society/EHSprojects.html#B2-8				
B2-9	Generation & Characterization of Nanoparticles		NIOSH/DART	
http://www.nano.gov/html/society/EHSprojects.html#B2-9				
<u>NSF</u>	<u>Extramural</u>			
B2-10	NIRT: Design of Biocompatible Nanoparticles for Probing Living Cellular Functions and their Potential Environmental Impacts	0507036	Old Dominion University Research Foundation	
http://www.nano.gov/html/society/EHSprojects.html#B2-10				
B2-11	NER: Novel Cell Culture Stylus for the Rapid Assessment of Functional Nano-bio Interfaces	0609311	University of Florida	
http://www.nano.gov/html/society/EHSprojects.html#B2-11				
B2-12	SGER: Aquatic Nanotoxicology of Nanomaterials and their Biomolecular Derivatives	0630823	Clemson University	
http://www.nano.gov/html/society/EHSprojects.html#B2-12				
B2-13	NSEC: Center for Affordable Nanoengineering	0425626	Ohio State University	The goal of this center is to design and fabricate nanofluidic circuits for manipulating individual biomolecules. The EHS focus of this work lies in designing and assessing transport and biocompatibility of various nanostructures in the test system. Biocompatibility issues will be addressed in parallel with the development of new nano-fluidic designs and devices.
http://www.nano.gov/html/society/EHSprojects.html#B2-13				

No. of Projects: 6

Establish the relationship between the properties of nanomaterials and uptake via the respiratory or digestive tracts or through the eyes or skin, and assess body burden

Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>EPA</u>	<u>Extramural</u>			
B3-1	A Rapid In Vivo System for Determining Toxicity of Manufactured Nanomaterials	RD-833320	Oregon State University	
http://www.nano.gov/html/society/EHSprojects.html#B3-1				
<u>NIH</u>	<u>Extramural</u>			

Abstract #	Project	Award ID	Lead Institution	Additional Notes
B3-2	Polymer-nucleotide Complexes With Cytotoxic Activity	5R01CA102791-04	University of Nebraska Medical Center	The goal of this project is to develop targeted nano-probes for molecular imaging to enable non-invasive early detection of cancer. The EHS relevant component of this research involves the pharmacokinetic testing of nano-probes (linking peptide targets to a variety of nanostructures) in mouse models to identify the best candidate nanoprobe for clinical evaluation.
http://www.nano.gov/html/society/EHSprojects.html#B3-2				
B3-3	Detecting Cancer Early With Targeted Nano-probes for Va*	5R01CA119414-02	University of California-San Francisco	The goal of this grant is to develop hybrid gold-nanoparticle-based molecular imaging and therapeutic agents for diagnosis and treatment of prostate cancer. The EHS relevant component of this research includes characterization and study of photophysical properties, size, dispersity, biolocalization, pharmacokinetics and in vivo profiles of stabilized gold nanoparticles.
http://www.nano.gov/html/society/EHSprojects.html#B3-3				
B3-4	Hybrid Nanoparticles In Imaging and Therapy of Prostate*	5R01CA119412-02	University of Missouri-Columbia	The EHS relevance of this research is development and implementation of techniques to detect and characterize genetic damage that may result from a variety of chemicals and materials in the environment, including carbon nanotubes.
http://www.nano.gov/html/society/EHSprojects.html#B3-4				
B3-5	Development of Methods and Models for Nanoparticle Toxicity Screening: Applicatio	1R01ES015498-01	University of California-Los Angeles	The goal of this project is to develop novel cytotoxic nucleotide drugs embedded in a nanoscale polymer carriers that help stabilize, protect and target the drug. The EHS relevant component of this research is to determine whether the polymer-nucleotide complexes can increase the cytotoxic effects of the non-encapsulated nucleotide analogues.
http://www.nano.gov/html/society/EHSprojects.html#B3-5				
<u>USDA (CSREES) Extramural</u>				
B3-6	Role of Chromosome Alterations In Environmental Carcinogenesis	CA-R*-NEU-7524-H	University of California-Riverside	
http://www.nano.gov/html/society/EHSprojects.html#B3-6				
<hr/>				
No. of Projects: 11	<i>Determine the mechanisms of interaction between nanomaterials and the body at the molecular, cellular, and tissular levels</i>			
<hr/>				
Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>NIH Extramural</u>				
B4-1	Treatment of Type 2 Diabetes With Oral Administration of Nanoencapsulated Glp-1	1R43DK075190-01	Therapyx, Inc	This research seeks to optimize a system for non-invasive administration of medication encapsulated in nanoparticles. Dosage and kinetic studies are a major research thrust.
http://www.nano.gov/html/society/EHSprojects.html#B4-1				

Appendix A. FY 2006 Nanotechnology-Related EHS Research Projects

Abstract #	Project	Award ID	Lead Institution	Additional Notes
B4-2	Pharmokinetics of Therapeutic Antibody-targeted Gold Nanoparticles	3U10HD037242-08S	Baylor College of Medicine	
				http://www.nano.gov/html/society/EHSprojects.html#B4-2
B4-3	Apply Nanotechnology To Targeted Drug Delivery Across Blood Brain Barrier	5U10HD037261-07	Wayne State University	
				http://www.nano.gov/html/society/EHSprojects.html#B4-3
B4-4	UTEP-UNM HSC Arch Program On Border Asthma	5S11ES013339-02	University of Texas-El Paso	This work seeks to develop data relating ultrafine (less than 100 nanometer) air particulate contamination with asthma causation. Baseline information on the characteristics of ultrafine particles will be developed, including specific focus on occurrence of carbon nanotubes in kitchens and in vitro data on inflammatory measures following carbon nanotube exposure.
				http://www.nano.gov/html/society/EHSprojects.html#B4-4
B4-5	Skin Penetration, Phototoxicity, and Photocarcinogenesis of Nanoscale Oxides of Titanium and Zinc	E2156_NCTR		
				http://www.nano.gov/html/society/EHSprojects.html#B4-5
B4-6	Toxicokinetics of Quantum Dots In Rats			
				http://www.nano.gov/html/society/EHSprojects.html#B4-6
B4-7	Toxicokinetic Studies of Fullerene C60	1R01ES015498-01	University of California-Los Angeles	
				http://www.nano.gov/html/society/EHSprojects.html#B4-7
<u>NIOSH</u>		<u>Intramural</u>		
B4-8	Role of CNT's In Cardiovascular Inflammation & Copd Related Diseases		NIOSH/HELD	
				http://www.nano.gov/html/society/EHSprojects.html#B4-8
B4-9	Dermal Effects of Nanoparticles		NIOSH/HELD	
				http://www.nano.gov/html/society/EHSprojects.html#B4-9
B4-10	Pulmonary Deposition and Translocation of Nanomaterials		NIOSH/HELD	
				http://www.nano.gov/html/society/EHSprojects.html#B4-10
<u>NSF</u>		<u>Extramural</u>		
B4-11	Biochemical, Molecular and Cellular Responses of Zebrafish Exposed To Metallic Nanoparticles	0540920	University of Florida	
				http://www.nano.gov/html/society/EHSprojects.html#B4-11

No. of Projects: 39		<i>Identify or develop appropriate in vitro and in vivo assays/models to predict in vivo human responses to nanomaterials exposure</i>		
Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>DOD (AFOSR)</u> <u>Extramural</u>				
B5-2	Safer Nanomanufacturing		ONAMI	
http://www.nano.gov/html/society/EHSprojects.html#B5-2				
B5-3	Identifying Critical P-C Characteristics of Np That Elicit Toxic Effects	CA-R*-NEU-7524-H	University of California-Riverside	The EHS portion of the goal of this grant is to determine the relationship between the toxicity and physicochemical characteristics of nanoparticle by developing methodologies to characterize nanoparticles and test nanomaterials for toxicity using in vitro and in vivo techniques.
http://www.nano.gov/html/society/EHSprojects.html#B5-3				
<u>DOD (AFOSR)</u> <u>Intramural</u>				
B5-1	Biological Interaction of Nanomaterials			
http://www.nano.gov/html/society/EHSprojects.html#B5-1				
<u>EPA</u> <u>Extramural</u>				
B5-4	Effects of Ingested Nanoparticles On Gene Regulation In The Colon	R833336	University of Utah	
http://www.nano.gov/html/society/EHSprojects.html#B5-4				
<u>NIH</u> <u>Extramural</u>				
B5-5	Design of Targeting Enhancement for Drug Delivery	5R21CA112436-02	Case Western Reserve University	This project tests nanomaterials in in vitro binding study and cell uptake study
http://www.nano.gov/html/society/EHSprojects.html#B5-5				
B5-6	Using Viral Nanoparticles To Target Cancer	5R01CA112075-03	Scripps Research Institute	The EHS component investigates the behaviors of viral nanoparticles in vivo.
http://www.nano.gov/html/society/EHSprojects.html#B5-6				
B5-7	Pharmacology of Targeted Therapy To Brain Tumors	5R01CA107268-04	University of California-San Francisco	The goal of this grant is to develop non-viral gene nanoparticle carriers to target brain tumors. The EHS-relevant component of this research is to characterize the factors that optimize the ability of nanolipoparticles to target brain tumors and enhance the therapeutic efficacy of nanolipoparticles using in vitro and in vivo techniques.
http://www.nano.gov/html/society/EHSprojects.html#B5-7				
B5-8	Nanotechnology Platform for Pediatric Brain Cancer Image	5R01CA119408-02	University of Washington	The goal of this grant is to develop tumor targeting nanoparticle agents to improve the diagnosis and treatment of brain cancer in children. The EHS-relevant component of this research is to develop multifunctional nanoparticle agents that target brain tumors and characterize the factors that optimize the therapeutic efficacy and delivery of these nanoparticles to brain tumors using in vitro and in vivo techniques.
http://www.nano.gov/html/society/EHSprojects.html#B5-8				

Appendix A. FY 2006 Nanotechnology-Related EHS Research Projects

Abstract #	Project	Award ID	Lead Institution	Additional Notes
B5-9	Multifunctional Nanoparticles for Targeted DNA Vaccine Delivery	1R21CA121832-01	University of Minnesota-Twin Cities	The goal of this grant is to develop a platform DNA vaccine delivery technology based on rationally designed polymer-based nanostructures that will have a significant impact on gene-based immunotherapy for treating cancer and infectious diseases. The EHS-relevant component of this research is to synthesize biodegradable multifunctional polymer nanoparticles and evaluate their efficacy and efficiency using in vivo and in vitro techniques.
http://www.nano.gov/html/society/EHSprojects.html#B5-9				
B5-10	Novel Lentiviral Packaging Systems	5R01DK065939-03	Brigham And Women's Hospital	A portion of this grant will examine the interaction of Nanomaterials with viral particles.
http://www.nano.gov/html/society/EHSprojects.html#B5-10				
B5-11	Translational Program of Excellence In Nanotechnology	5U01HL080731-03	Massachusetts General Hospital	The goal of this project is to develop nanotechnology application for better diagnosis and treatment of heart, lung, blood and sleep disorders. The EHS-relevant component is to develop multidimensional cell screens to rapidly and sensitively test biosafety of novel materials.
http://www.nano.gov/html/society/EHSprojects.html#B5-11				
B5-12	Designing ECM-inspired Peptide Biomaterials for Regenerative Medicine	1R21DE017703-01	University of Cincinnati	The goal of this project is to engineer new biomaterials formulated from self-assembling peptides or peptidomimetics to produce synthetic extracellular matrices useful for tissue repair or regeneration. The EHS-relevant component is to understand the humoral and cellular immunologic response to the multimerizing peptides.
http://www.nano.gov/html/society/EHSprojects.html#B5-12				
B5-13	New Nanoparticles for Antimicrobial Therapy of Dental Plaque Related Diseases	1R43DE017505-01	Lynntech, Inc.	The goal of this project is to develop a new antimicrobial photodynamic therapy based on nanomaterials for the treatment of oral diseases. The EHS-relevant component is to conduct cytotoxicity assays of the fullerene photosensitizers.
http://www.nano.gov/html/society/EHSprojects.html#B5-13				
B5-14	Nanotechnology In Osseointegration of TMJ Implants	5R01DE013952-06	University of Alabama at Birmingham	In this grant, in vivo biocompatibility testing of nanostructured diamond and calcium phosphate ceramics will be carried out using standardized model systems, including injection of particulate debris, plus soft and hard tissue evaluations of particulates and implants.
http://www.nano.gov/html/society/EHSprojects.html#B5-14				
B5-15	Complex Nanocomposites for Bone Regeneration	5R01DE015633-04	Lawrence Berkeley National Laboratory	The goal of this project is to develop hydroxyapatite crystal structures for bone mineralization. The EHS-relevant component is to test new composite materials in vitro in cell cultures and in vivo in an animal model. The behavior of the developed new composite material will be tested in vitro in cell cultures.
http://www.nano.gov/html/society/EHSprojects.html#B5-15				

Appendix A. FY 2006 Nanotechnology-Related EHS Research Projects

Abstract #	Project	Award ID	Lead Institution	Additional Notes
B5-16	Biomimetic Scaffold for Bone-Repair	5R01DE016533-03	University of Illinois-Chicago	This grant will assess the immune response to the new peptide amphiphiles single-branched RODS nanofiber gels were transplanted intraperitoneally in isogenic C57BL/6 strain mice.
http://www.nano.gov/html/society/EHSprojects.html#B5-16				
B5-17	Nanotechnology Strategies for Growth of Bones and Teeth	5R01DE015920-02	Northwestern University	The goal of this project is to develop peptide nanostructures for bone mineralization. The EHS-relevant component is to test overall biocompatibility and biodegradation of peptide nanostructures.
http://www.nano.gov/html/society/EHSprojects.html#B5-17				
B5-18	Nanocoatings for Biomedical Implants	5R43DE015730-02	Nanomech, LLC	The goal of this project is to develop a nanoparticle coating of hydroxyapatite on titanium dental implants. Biocompatibility of the coated dental implants and effects on osteoblast adhesion will be tested in cell cultures and compared with samples without HAP coating.
http://www.nano.gov/html/society/EHSprojects.html#B5-18				
B5-19	Center of Excellence In Translational Human Stem Cell Research; Investigating the Effects of Nanogels On hESC and Then Using Those for Regeneration	5P50NS054287-02	Northwestern University	The EHS component assesses bioactive peptide amphiphiles that can self-assemble into nanofiber scaffolds for use in cell culture and delivery.
http://www.nano.gov/html/society/EHSprojects.html#B5-19				
B5-20	Nanoparticles As Promoters of Cell Longevity	5R01AG022617-04	Virginia Polytechnic Institute And State University	
http://www.nano.gov/html/society/EHSprojects.html#B5-20				
B5-21	Nano-apatite Coating of the Porous Surface of Implants	5R43AR051249-02	Nano Interface Technology, Inc	The EHS component will test the biocompatibility and toxicity of unagglomerated nanoparticles of the carbonated hydroxyapatite as well as of coating Ti-alloy with nanoparticles of carbonated hydroxyapatite that are used in implanted devices.
http://www.nano.gov/html/society/EHSprojects.html#B5-21				
B5-22	The Interaction of Polycationic Organic Polymers With Biological Membranes	1R01EB005028-01A2	University of Michigan-Ann Arbor	The goal of this research is to understand the basic mechanisms for delivery of nano-scale materials in biological systems. The EHS-relevant component of this research will be the elucidation of interactions between nano-scale materials (some engineered, some not) and cellular components within biological systems.
http://www.nano.gov/html/society/EHSprojects.html#B5-22				
B5-23	Reconfigurable Nanoengineered Extracellular Matrices	5R21EB003793-03	University of Michigan-Ann Arbor	This project will generate some engineered nano and cell proliferation data.
http://www.nano.gov/html/society/EHSprojects.html#B5-23				
B5-24	Stimulus-Responsive, Mechanically-Dynamic Nanocomposite for Cortical Electrodes; Developing Polymer and Investigating the Tissue Response	1R21NS053798-01A	Case Western Reserve University	The EHS component will test the chronic astrocytic and tissue response to a polymer nanocomposite.
http://www.nano.gov/html/society/EHSprojects.html#B5-24				

Appendix A. FY 2006 Nanotechnology-Related EHS Research Projects

Abstract #	Project	Award ID	Lead Institution	Additional Notes
B5-25	Mechanisms of Orthopedic Implant Osteolysis	3R01AR032788-19S1	Barnes-Jewish Hospital	This grant studies the mechanism of orthopedic implant osteolysis and other forms of inflammation-induced bone loss to understand the mechanisms of interaction between nanomaterials and the body at the molecular, cellular and tissue levels, and may have value for broader understanding of interactions between engineered nanomaterials and biological components.
http://www.nano.gov/html/society/EHSprojects.html#B5-25				
B5-27	Imaging Nanocomposites Targeting Tumor Microvasculature	5R01CA104479-02	Roswell Park Cancer Institute Corp	This project will provide information on functionalized nanogold.
http://www.nano.gov/html/society/EHSprojects.html#B5-27				
B5-28	Nanoparticle Disruption of Cell Function	1R01ES015497-01	University of Montana	This research is geared towards understanding interactions between engineered nanomaterials and various biological components.
http://www.nano.gov/html/society/EHSprojects.html#B5-28				
B5-29	Inhalation Toxicity of Fullerene C60	1R01ES015495-01	New York University School of Medicine	This research is geared towards understanding interactions between engineered nanomaterials and various biological components, both at molecular and cellular levels.
http://www.nano.gov/html/society/EHSprojects.html#B5-29				
B5-30	Tumorigenicity of Photoactive Nanoscale Titanium Dioxide In Tg.ac Transgenic Mice			Research performed by the National Toxicology Program will provide improved understanding of biological mechanisms and interactions of engineered nanomaterials. The research will also enhance scientific knowledge of how such materials are transported within and between biological components.
http://www.nano.gov/html/society/EHSprojects.html#B5-30				
B5-32	Micellar Vip Nanoparticles for Rheumatoid Arthritis	5R01AG024026-03	University of Illinois-Chicago	This grant will test the ability of a disease-related molecule to self-associate with 17nm phospholipid particles and will examine biocompatibility and biodegradability. The EHS research will explore how proteins interact with nanovesicles.
http://www.nano.gov/html/society/EHSprojects.html#B5-32				
B5-33	Curcumin and Curcumin Derivatives for Alzheimer's	1U01AG028583-01	Sepulveda Research Corporation	A portion of this grant will evaluate the efficacy, bioavailability, and toxicity of a curcumin lipid nanoparticles in vivo.
http://www.nano.gov/html/society/EHSprojects.html#B5-33				
B5-34	Systemic Implications of Total Joint Replacement	5R01AR039310-15	Rush University Medical Center	This grant investigates metallic degradation products of total joint replacement to understand the mechanisms of interaction between nanomaterials and the body at the molecular, cellular and tissue levels.
http://www.nano.gov/html/society/EHSprojects.html#B5-34				
B5-35	Long Term Cardiovascular Effects of Inhaled Nanoparticles	1R01ES015495-01	New York University School of Medicine	
http://www.nano.gov/html/society/EHSprojects.html#B5-35				

NIH

Intramural

Abstract #	Project	Award ID	Lead Institution	Additional Notes
B5-26	Nanotechnology Characterization Laboratory			Research performed at this laboratory will provide improved understanding of biological mechanisms and interactions of engineered nanomaterials, enhance scientific knowledge of how such materials are transported within and between biological components.
http://www.nano.gov/html/society/EHSprojects.html#B5-26				
B5-31	Mechanisms of Chemically Induced Photosensitivity	1Z01ES050046-28	NIEHS-Laboratory of Pharmacology	This research is geared towards understanding interactions between engineered nanomaterials and various biological components at molecular, cellular and tissular levels.
http://www.nano.gov/html/society/EHSprojects.html#B5-31				
<u>NIOSH</u>		<u>Extramural</u>		
B5-38	Lung Oxidative Stress/inflammation By Carbon Nanotubes	1R01OH008282-01A	University of Pittsburgh	
http://www.nano.gov/html/society/EHSprojects.html#B5-38				
<u>NIOSH</u>		<u>Intramural</u>		
B5-36	Pulmonary Toxicity of Carbon Nanotube Particles		NIOSH/HELD	
http://www.nano.gov/html/society/EHSprojects.html#B5-36				
B5-37	Systematic Microvascular Dysfunction Effects of Ultrafine Versus Fine Particles		NIOSH/HELD	This research will identify cardiovascular effects in rats after inhalation of fine TiO ₂ particles and nanoparticles. The EHS-relevant component will measure markers of pulmonary inflammation and systemic microvascular dysfunction.
http://www.nano.gov/html/society/EHSprojects.html#B5-37				
<u>NSF</u>		<u>Extramural</u>		
B5-39	NIRT: Controlling Interfacial Activity of Nanoparticles: Robust Routes To Nanoparticle-based Capsules, Membranes, and Electronic Materials	0609107	University of Massachusetts-Amherst	Portions of the funding are targeted to using nanoparticles and self-assembly for development of release systems for therapeutic drug treatments, and to development of nanostructured membranes for water purification and filtration.
http://www.nano.gov/html/society/EHSprojects.html#B5-39				
<hr/>				
No. of Projects: 1	<i>Addresses Research Needs In Nanomaterials and Human Health Not Captured in Priority Needs 1-5</i>			
Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>NIOSH</u>		<u>Intramural</u>		
B7-2	Nanotechnology Safety and Health Coordination		NIOSH/HELD	
http://www.nano.gov/html/society/EHSprojects.html#B7-2				

Nanomaterials and the Environment

No. of Projects: 5

Understand the effects of engineered nanomaterials in individuals of a species and the applicability of testing schemes to measure effects

Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>EPA</u>		<u>Extramural</u>		
C1-1	Methodology Development For Manufactured Nanomaterial Bioaccumulation Test	R8333327	Arizona State University	This project will evaluate the influence of bioconcentration, bioaccumulation, and biomagnification of manufactured nanomaterials in a simulated food chain and aquatic organisms consisting of algae, daphnia, and zebrafish.
http://www.nano.gov/html/society/EHSprojects.html#C1-1				
C1-2	The Effect Of Surface Coatings On The Environmental And Microbial Fate Of Nanoiron And Fe-oxide Nanoparticles	R833326	Carnegie Mellon University	The study objectives are to determine the effect of common NP surface coatings on nanoiron and nanoiron-oxide reactivity, mobility, fate, and their effect on soil bacteria.
http://www.nano.gov/html/society/EHSprojects.html#C1-2				
C1-3	Aquatic Toxicity Of Waste Stream Nanoparticles	RD833317	NYU School of Medicine	This project will investigate particle-type dependent differences in the developmental toxicity of manufactured nanoparticles in aquatic species.
http://www.nano.gov/html/society/EHSprojects.html#C1-3				
<u>NSF</u>		<u>Extramural</u>		
C1-4	Biochemical, Molecular And Cellular Responses Of Zebrafish Exposed To Metallic Nanoparticles	0540920	University of Florida	One objective of this project is to compare toxicity of metals to zebrafish in the dissolved and nanoparticle state as well as the nanoparticles of different sizes and shape. In vitro work will also be done.
http://www.nano.gov/html/society/EHSprojects.html#C1-4				
<u>USDA (CSREES)</u>		<u>Extramural</u>		
C1-5	Cellular And Materials-based Studies Of Marine Invertebrates To Advance Biomineralization, Antifouling And Nanotechnology Fields	SC-1700288	Clemson University	This grant will examine cellular and/or whole organism responses to nanomaterials. Molluscs, daphnia, and fat head minnows will be examined for toxicity, larval settlement and attachment processes, and apoptosis.
http://www.nano.gov/html/society/EHSprojects.html#C1-5				

No. of Projects: 1

Understand environmental exposures through identification of principle sources of exposure and exposure routes

Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>NSF</u>		<u>Extramural</u>		
C2-1	Environmental Molecular Science Institute: Actinides And Heavy Metals In The Environment - The Formation, Stability, And Impact Of Nano- Micro-Particles	0221966	University of Notre Dame	
http://www.nano.gov/html/society/EHSprojects.html#C2-1				

<i>Evaluate abiotic and ecosystem-wide effects</i>				
No. of Projects: 1				
Abstract #	Project	Award ID	Lead Institution	Additional Notes
NSF	Extramural			
C3-1	NER: Nanoscale Size Effects On The Biogeochemical Reactivity Of Iron Oxides In Active Environmental Nanosystems	0608749	Washington University	This project will provide information on the effect of naturally-occurring nanoparticles on the biogeochemical cycling of metals of concern in the subsurface.
http://www.nano.gov/html/society/EHSprojects.html#C3-1				
<i>Determine factors affecting the environmental transport of nanomaterials</i>				
No. of Projects: 22				
Abstract #	Project	Award ID	Lead Institution	Additional Notes
DOD (AFOSR)	SBIR			
C4-1	Measure The Transport Of Modified Nanoparticles Through Soil	FA8651-06-C-0136	nanoComposix	nanoComposix will investigate the fate, transport, and compartmentalization of nanoparticles in the environment. The transport and toxicology of commercially available powered aluminum and tantalum nanoparticles will be compared to precisely engineered nanoparticles.
http://www.nano.gov/html/society/EHSprojects.html#C4-1				
DOE	Extramural			
C4-2	How Do Interfacial Phenomena Control Nanoparticle Structure?		University of California-Berkeley	This project will provide information on stability and transformation processes which may help inform understanding of environmental transport.
http://www.nano.gov/html/society/EHSprojects.html#C4-2				
C4-3	Frontiers In Biogeochemistry And Nanomineralogy: Studies In Quorum Sensing And Nanosulfide Dissolution Rates		Virginia Polytechnic Institute And State University	This work will provide information on stability and transformation processes which may help inform our understanding of environmental transport.
http://www.nano.gov/html/society/EHSprojects.html#C4-3				
C4-4	How Do Interfacial Phenomena Control Nanoparticle Structure?		University of California-Davis	This work will provide information on stability and transformation processes which may help inform our understanding of environmental transport.
http://www.nano.gov/html/society/EHSprojects.html#C4-4				
EPA	Extramural			
C4-5	Ecotoxicology Of Underivatized Fullerenes (C60) In Fish	R833333	University of Tennessee - Knoxville	This work will provide information on stability and transformation processes which may help inform our understanding of environmental transport.
http://www.nano.gov/html/society/EHSprojects.html#C4-5				
C4-6	Carbon Nanotubes: Environmental Dispersion States, Transport, Fate, And Bioavailability	R833321	University of Michigan-Ann Arbor	
http://www.nano.gov/html/society/EHSprojects.html#C4-6				

Abstract #	Project	Award ID	Lead Institution	Additional Notes
C4-7	Biological Fate And Electron Microscopy Detection Of Nanoparticles During Wastewater Treatment	R833322	Arizona State University	
http://www.nano.gov/html/society/EHSprojects.html#C4-7				
<u>NIH</u>		<u>Extramural</u>		
C4-8	Sub-micrometer Zero Valent Metal For In-Situ Remediation Of Contaminated Aquifers	1R43ES014114-01A1	OnMaterials, LLC0	
http://www.nano.gov/html/society/EHSprojects.html#C4-8				
<u>NSF</u>		<u>Extramural</u>		
C4-9	CAREER: Carbonaceous Particles Of Tarry Origin	0349282	University of Illinois-Urbana-Champaign	This research will characterize the physical and chemical properties of carbonaceous particles generated in the combustion of solid fuels
http://www.nano.gov/html/society/EHSprojects.html#C4-9				
C4-10	NIRT: Metal Ion Complexation By Dendritic Nanoscale Ligands: Fundamental Investigations And Applications To Water Purification	0506951	Howard University	This project will examine dendrimer binding of metals.
http://www.nano.gov/html/society/EHSprojects.html#C4-10				
C4-11	SGER: Particle Incorporation Of PAH In Aquatic Environments: Implications To Fate And Transport	0610537	Rensselaer Polytechnic Institute	
http://www.nano.gov/html/society/EHSprojects.html#C4-11				
C4-12	SGER: Metallic Nanocatalysts For Rapid Transformation Of Polychlorinated Dibenzo-p-dioxins	0636820	Rutgers University New Brunswick	
http://www.nano.gov/html/society/EHSprojects.html#C4-12				
C4-13	Center Of Advanced Materials For Purification Of Water With Systems	0120978	University of Illinois-Urbana-Champaign	This research will study water processing and the Angstrom to nanometer scale interactions between aqueous solutions and solid substrates for separation/transformation of compounds in water.
http://www.nano.gov/html/society/EHSprojects.html#C4-13				
C4-14	CAREER: Interfacial Reactions Affecting Heavy Metal Fate And Transport: An Integrated Research And Education Plan	0546219	Washington University	
http://www.nano.gov/html/society/EHSprojects.html#C4-14				
C4-15	Carbon Nanoparticles In Combustion: A Multiscale Perspective	0553764	University of Michigan-Ann Arbor	
http://www.nano.gov/html/society/EHSprojects.html#C4-15				

Abstract #	Project	Award ID	Lead Institution	Additional Notes
C4-16	Development Of A Copolymer-based System For Targeted Delivery Of Nanoparticulate Iron To Environmental Non-Aqueous Phase Liquids	0521721	Carnegie Mellon University	This project will include transport of iron nanoparticles in the subsurface
http://www.nano.gov/html/society/EHSprojects.html#C4-16				
C4-17	Aggregation And Deposition Behavior Of Carbon Nanotubes In Aquatic Environments	0646247	Yale University	
http://www.nano.gov/html/society/EHSprojects.html#C4-17				
<u>USDA (CSREES) Extramural</u>				
C4-18	Reactivity, Aggregation And Transport Of Nanocrystalline Sesquioxides In The Soil System	CALR-2006-02656	University of California	
http://www.nano.gov/html/society/EHSprojects.html#C4-18				
C4-19	Colloid Interfacial Reactions In Open Microchannel Representing Unsaturated Soil Capillaries	DEL00622	University of Delaware	This project will provide information on stability and transformation processes which may help inform understanding of environmental transport.
http://www.nano.gov/html/society/EHSprojects.html#C4-19				
C4-20	Elucidating Interactions And Transformations Of Pollutants And Organic Matter In Soil	MO-NRSL0728	University of Missouri	This research will focus on the transformation processes and nanopore effects on organic compound sorption and retention to mineral surfaces.
http://www.nano.gov/html/society/EHSprojects.html#C4-20				
C4-21	Conference Symposium: Environmental Mineralogy And Toxic Metals	NC09323	North Carolina State University	
http://www.nano.gov/html/society/EHSprojects.html#C4-21				
C4-22	Sorption And Availability Of Metals And Radionuclides In Soils	WNP00385	Washington State University	
http://www.nano.gov/html/society/EHSprojects.html#C4-22				

No. of Projects: 9

Understand the transformation of nanomaterials under different environmental conditions

Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>DOE Extramural</u>				
C5-1	Experimental, Theoretical, And Model-based Studies Of Crystallographically Controlled Self-assembly During Nanocrystal Growth		Lawrence Berkeley National Laboratory	This research will evaluate morphological transformation changes of nanocrystal growth in water and other media using zinc nanosulfides.
http://www.nano.gov/html/society/EHSprojects.html#C5-1				

NSF**Extramural**

Abstract #	Project	Award ID	Lead Institution	Additional Notes
C5-2	CAREER: An Integrated Research And Education Program In Long-term Durability Of Nano-structured Cement-based Materials During Environmental Weathering http://www.nano.gov/html/society/EHSprojects.html#C5-2	0547024	Vanderbilt University	
C5-3	CAREER: Gas-phase Catalytic Processes On Metal Nanoclusters http://www.nano.gov/html/society/EHSprojects.html#C5-3	0448491	University of Central Florida	This project studies the transformation of nanoparticles due to catalytic processes
C5-4	Investigating The Surface Structure And Reactivity Of Bulk And Nanosized Manganese Oxides http://www.nano.gov/html/society/EHSprojects.html#C5-4	0544246	University of Delaware	
C5-5	Environmental Biogeochemistry And Nanoscience: Applications To Toxic Metal Transport In The Environment http://www.nano.gov/html/society/EHSprojects.html#C5-5	0610373	NA	
C5-6	Collaborative Research: Fullerene Aggregation In Aquatic Systems http://www.nano.gov/html/society/EHSprojects.html#C5-6	0653659	Duke University	
C5-7	The Formation Rates And Structure Of Nanodroplets http://www.nano.gov/html/society/EHSprojects.html#C5-7	0518042	Ohio State University	
C5-8	NSEC: Center For Biological And Environmental Nanotechnology http://www.nano.gov/html/society/EHSprojects.html#C5-8	0647452	Rice University	This project encompasses a wide range of nanoparticle research including interaction of nanoparticles with biomolecules, polymer flow, and contaminant sorption
USDA (CSREES) Extramural				
C5-9	The Chemical And Physical Nature Of Particulate Matter Affecting Air, Water, And Soil Quality http://www.nano.gov/html/society/EHSprojects.html#C5-9	WNP00581	Washington State University	This work examines nanoparticles from agricultural emissions to air, water, and soil

No. of Projects: 11

Addresses Research Needs in Nanomaterials and the Environment Not Captured in Priority Needs 1-5

Abstract #	Project	Award ID	Lead Institution	Additional Notes
NSF Extramural				
C7-1	EPSCOR: New Mexico Research Program http://www.nano.gov/html/society/EHSprojects.html#C7-1	0447691	University of New Mexico	This work is focused on water sensing and purification, including studies of the nanomaterials-water interface.
C7-2	Reactive Membrane Technology For Water Treatment http://www.nano.gov/html/society/EHSprojects.html#C7-2	0403581	Northwestern University	

Appendix A. FY 2006 Nanotechnology-Related EHS Research Projects

Abstract #	Project	Award ID	Lead Institution	Additional Notes
C7-3	Magnetocaloric Effect In Nanoparticle Assemblies For Refrigeration Applications http://www.nano.gov/html/society/EHSprojects.html#C7-3	0408933	University of South Florida	
C7-4	EPSCOR: Delaware Research Infrastructure Improvement Program http://www.nano.gov/html/society/EHSprojects.html#C7-4	0447610	University of Delaware	This project has environmental and bionanotechnology components integrated with educational programs.
C7-5	EPSCOR: Alabama Research Infrastructure Improvement http://www.nano.gov/html/society/EHSprojects.html#C7-5	0447675	University of Alabama at Tuscaloosa	This statewide program will share facilities and bring together researchers (including environmental and material scientists) for collaborative work in biotechnology, nanotechnology, and sensing.
C7-6	NIRT: Active Nanoparticles In Nanostructured Materials Enabling Advances In Renewable Energy And Environmental Remediation http://www.nano.gov/html/society/EHSprojects.html#C7-6	0608896	University of Alabama at Tuscaloosa	
C7-7	NIRT: Actively Reconfigurable Nanostructured Surfaces For The Improved Separation Of Biological Macromolecules http://www.nano.gov/html/society/EHSprojects.html#C7-7	0608978	Rensselaer Polytechnic Institute	
C7-8	NIRT: Environmentally Benign Deagglomeration And Mixing Of Nanoparticles http://www.nano.gov/html/society/EHSprojects.html#C7-8	0506722	New Jersey Institute of Technology	
C7-9	CAREER: Hydroxyl Radical And Sulfate Radical-based Advanced Oxidation Nanotechnologies For The Destruction Of Biological Toxins In Water 7/1/05-6/30/10 http://www.nano.gov/html/society/EHSprojects.html#C7-9	0448117	University of Cincinnati	
C7-10	CAREER: On The Prevention Of Selenium And Arsenic Release Into The Atmosphere (2/15/05-1/31/09) http://www.nano.gov/html/society/EHSprojects.html#C7-10	0448758	Worcester Polytechnic Institute	
C7-11	Nanoscale Mineralogy And Geochemistry Of Arsenian Pyrite In Ore Deposits http://www.nano.gov/html/society/EHSprojects.html#C7-11	0537626	University of Michigan-Ann Arbor	

Health and Environmental Exposure Assessment

Characterize exposures among workers

No. of Projects: 2

Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>NIOSH</u>	<u>Intramural</u>			
D1-1	Nanotechnology Research Coordination		NIOSH/DART	The purpose of this project is to develop intramural surveys that will obtain fundamental data on workplace exposures related to nanotechnology.
http://www.nano.gov/html/society/EHSprojects.html#D1-1				
D1-2	Titanium Dioxide (TiO ₂) Nanoparticle Exposure Study		NIOSH/DSHEFS	
http://www.nano.gov/html/society/EHSprojects.html#D1-2				

Understand workplace processes and factors that determine exposure to nanomaterials

No. of Projects: 3

Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>DOD (AFOSR)</u>	<u>SBIR</u>			
D5-1	Small Business Innovation Research (SBIR): The Impact of Nanomaterials on Occupational Safety and Health			This project aims at identify factors that influence the generation, dispersion, and deposition of nanomaterials in the workplace.
http://www.nano.gov/html/society/EHSprojects.html#D5-1				
<u>NIOSH</u>	<u>Intramural</u>			
D5-2	Nanoparticles in the Workplace		NIOSH/DRDS	The purpose of this project is to foster the development of partnerships, exposure monitoring instrumentation, operational protocols, and a comprehensive and detailed database of nanoparticles and their properties aimed at providing the occupational safety and health community with a better understanding of the nature and extent of potential occupational exposures to nanoparticles.
http://www.nano.gov/html/society/EHSprojects.html#D5-2				
<u>NSF</u>	<u>Extramural</u>			
D5-3	Experimental and Numerical Simulation of the Fate of Airborne Nanoparticles from a Leak in a Manufacturing Process to Assess Worker Exposure	0646236	University of Minnesota-Twin Cities	
http://www.nano.gov/html/society/EHSprojects.html#D5-3				

Risk Management Methods

No. of Projects: 4

Understand and develop best workplace practices, processes, and environmental exposure controls

Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>NIOSH</u>	<u>Extramural</u>			
E1-4	Assessment Methods for Nanoparticles in the Workplace	1R01OH008806	University of Iowa	
http://www.nano.gov/html/society/EHSprojects.html#E1-4				
<u>NIOSH</u>	<u>Intramural</u>			
E1-1	Development and evaluation of nanofiber-based Filter Media		NIOSH/NPPTL	
http://www.nano.gov/html/society/EHSprojects.html#E1-1				
E1-2	Penetration of Nanoparticles through Respirator Filter Media		NIOSH/NPPTL	
http://www.nano.gov/html/society/EHSprojects.html#E1-2				
E1-3	Automobile Ultrafine Intervention		NIOSH/DART	
http://www.nano.gov/html/society/EHSprojects.html#E1-3				

No. of Projects: 2

Examine product or material life cycle to inform risk reduction decisions

Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>EPA</u>	<u>Extramural</u>			
E2-1	Comparative Life Cycle Analysis of Nano- and Bulk Materials in Photovoltaic Energy Generation	R833334	Columbia University	
http://www.nano.gov/html/society/EHSprojects.html#E2-1				
<u>NSF</u>	<u>Extramural</u>			
E2-2	The Life Cycle of Nanomanufacturing Technologies	0646336	University of Illinois-Chicago	
http://www.nano.gov/html/society/EHSprojects.html#E2-2				

No. of Projects: 1

Develop risk characterization information to determine and classify nanomaterials based on physical or chemical properties, and develop nanomaterial-use and safety-incident trend information to help focus risk management efforts

Abstract #	Project	Award ID	Lead Institution	Additional Notes
<u>NIOSH</u>	<u>Intramural</u>			
E3-1	Developing a Web-Based nano-Information Library		NIOSH/SRL	
http://www.nano.gov/html/society/EHSprojects.html#E3-1				

<i>Develop specific risk communication approaches and materials</i>				
No. of Projects: 1				
Abstract #	Project	Award ID	Lead Institution	Additional Notes
NIOSH	Intramural			
E5-1	Nanotechnology Information Dissemination		NIOSH/EID	
http://www.nano.gov/html/society/EHSprojects.html#E5-1				
<i>Overarching need: Evaluate risk management approaches for identifying and addressing risks from nanomaterials, and develop specific risk communication approaches and materials, and develop specific risk communication approaches and materials</i>				
No. of Projects: 6				
Abstract #	Project	Award ID	Lead Institution	Additional Notes
DOD (AFOSR)	SBIR			
E6-2	WINGS™- Web-Interfaced Nanotechnology ESH Guidance System for Force Health Protection	F071-033-1470	Luna Innovations	
http://www.nano.gov/html/society/EHSprojects.html#E6-2				
NSF	Extramural			
E6-1	NSEC: Center for Nanotechnology in Society at University of California, Santa Barbara	0531184	University of California-Santa Barbara	This research examines societal impacts, and develop cross discipline collaborative approaches including societal aspects, and risk perception concerning nanotechnology.
http://www.nano.gov/html/society/EHSprojects.html#E6-1				
E6-3	NSEC: Center for High Rate Nanomanufacturing	0425826	Northeastern University	This research includes risk management issues such as green design and net benefits analysis are incorporated in nanomanufacturing process evaluation and policy analysis.
http://www.nano.gov/html/society/EHSprojects.html#E6-3				
E6-4	NSEC: Center for Templated Synthesis and Assembly at the Nanoscale	0425880	University of Wisconsin-Madison	This research includes development of public engagement approaches and regulatory and risk management policy evaluation.
http://www.nano.gov/html/society/EHSprojects.html#E6-4				
E6-5	NIRT: Nanotechnology in the Public Interest: Regulatory Challenges, Capacity, & Policy Recommendations	0609078	Northeastern University	This research includes development of public engagement approaches, regulatory and risk management policy evaluation, and education relevant to risk management policy development.
http://www.nano.gov/html/society/EHSprojects.html#E6-5				
E6-6	NIRT: Evaluating Oversight Models for Active Nanostructures and Nanosystems: Learning from Past Technologies in a Societal Context	0608791	University of Minnesota-Twin Cities	This research evaluates risk management oversight approaches as they apply to nanoscale materials.
http://www.nano.gov/html/society/EHSprojects.html#E6-6				

Appendix B. Glossary

ADME	Absorption, distribution, metabolism, elimination
AF	(U.S.) Air Force
AFOSR	Air Force Office of Scientific Research
CDC	Centers for Disease Control and Prevention
CNT	Carbon nanotube
CPSC	Consumer Product Safety Commission
CSREES	Cooperative State Research, Education, and Extension Service (USDA)
DHHS	(Department of) Health and Human Services
DOD	Department of Defense
DOE	Department of Energy
DOT	Department of Transportation
EHS	Environmental, health, and safety
EPA	Environmental Protection Agency
ERDC	Engineer Research and Development Center (U.S. Army)
FDA	Food and Drug Administration (DHHS)
FY	Fiscal Year
GI	Gastrointestinal
ICON	International Council on Nanotechnology
ISO	International Organization for Standardization
LCA	Life cycle assessment
MRI	Magnetic resonance imaging
NCI	National Cancer Institute (NIH/DHHS)
NCL	Nanotechnology Characterization Lab (NCI/NIH/DHHS)
NEHI	Nanotechnology Environmental and Health Implications Working Group of the NSET
NIEHS	National Institute of Environmental Health Sciences (NIH/DHHS)
NIH	National Institutes of Health (DHHS)
NIL	Nanoparticle Information Library (NIOSH)
NIOSH	National Institute for Occupational Safety and Health (CDC/DHHS)
NIST	National Institute of Standards and Technology (DOC)
NNCO	National Nanotechnology Coordination Office

Appendix B. Glossary

NNI	National Nanotechnology Initiative
NSET	Nanoscale Science, Engineering, and Technology Subcommittee of the NSTC
NSF	National Science Foundation
NSTC	National Science and Technology Council
OECD	Organisation for Economic Co-operation and Development
OSHA	Occupational Safety and Health Administration
PCA	Program Component Area (of the NNI Strategic Plan)
PET	Positron emission tomography
RMM	Risk Management Methods
SBIR	Small Business Innovation Research (multiagency Federal program)
TC 229	Technical Committee on Nanotechnologies of the ISO
USDA	United States Department of Agriculture
USGS	United States Geological Survey (Department of the Interior)
WPMN	Working Party on Manufactured Nanomaterials of the OECD

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